

FIG. 1

b. a. \ominus



\oplus

FIG 2

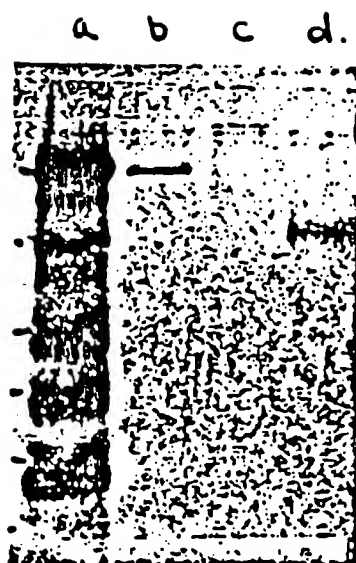


FIG. 3

a b c d.

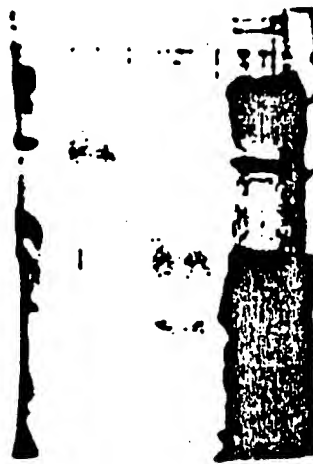


FIG 4

a. b.

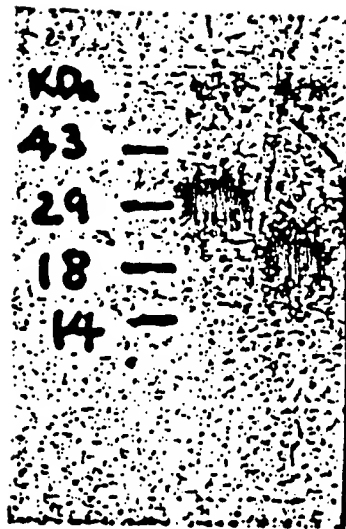
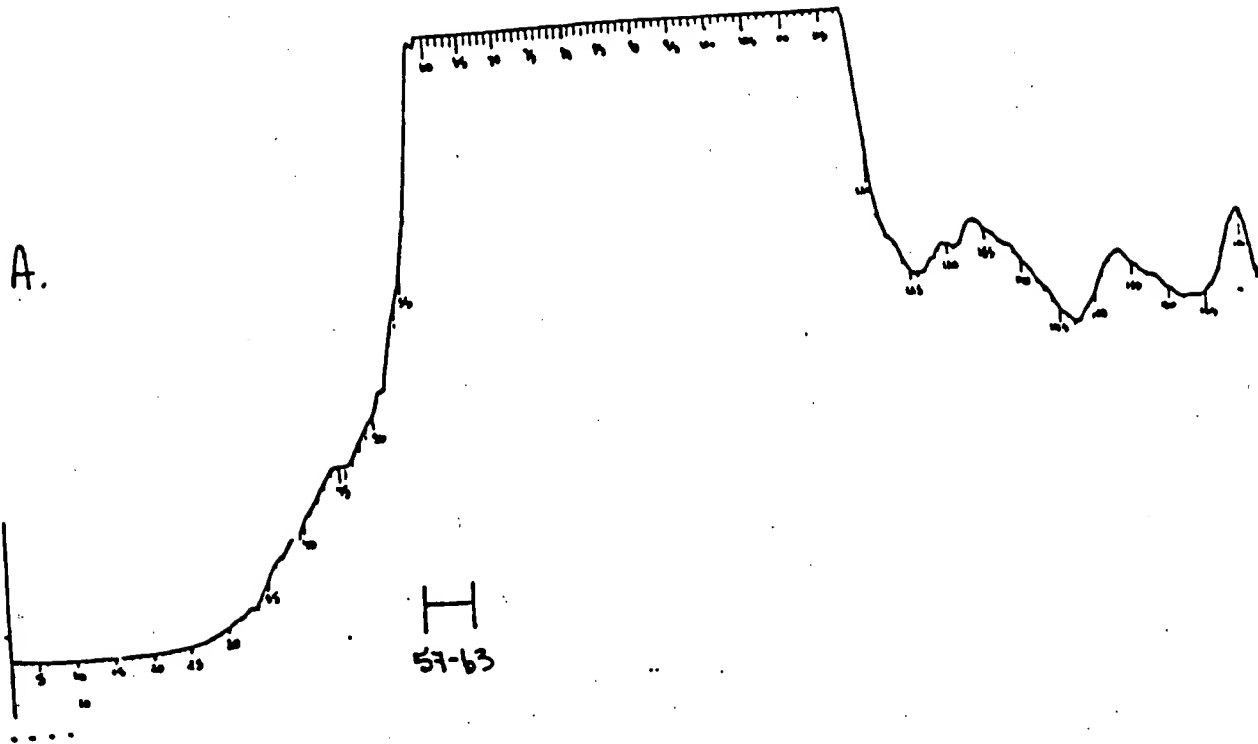


FIG. 5

Figure 6

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B.

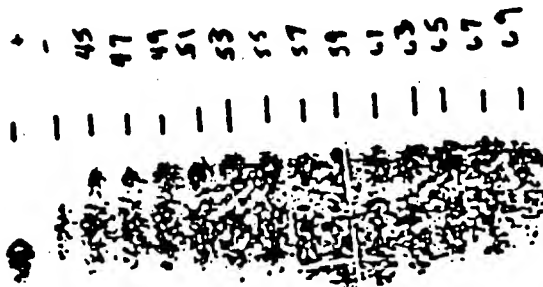
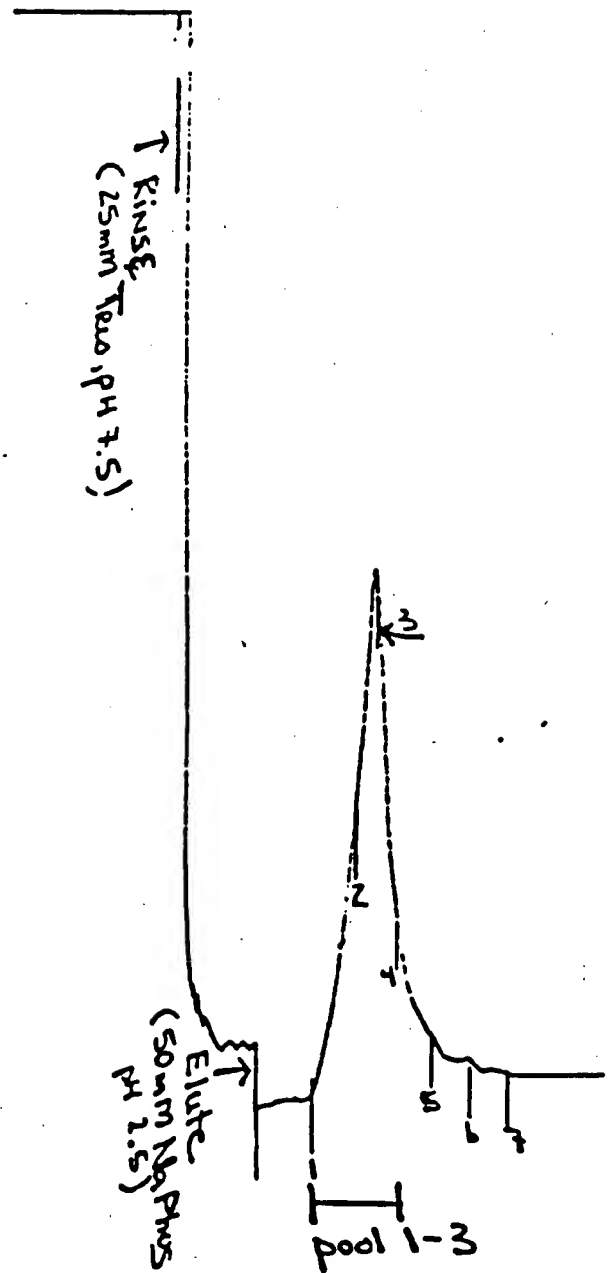


Figure 7



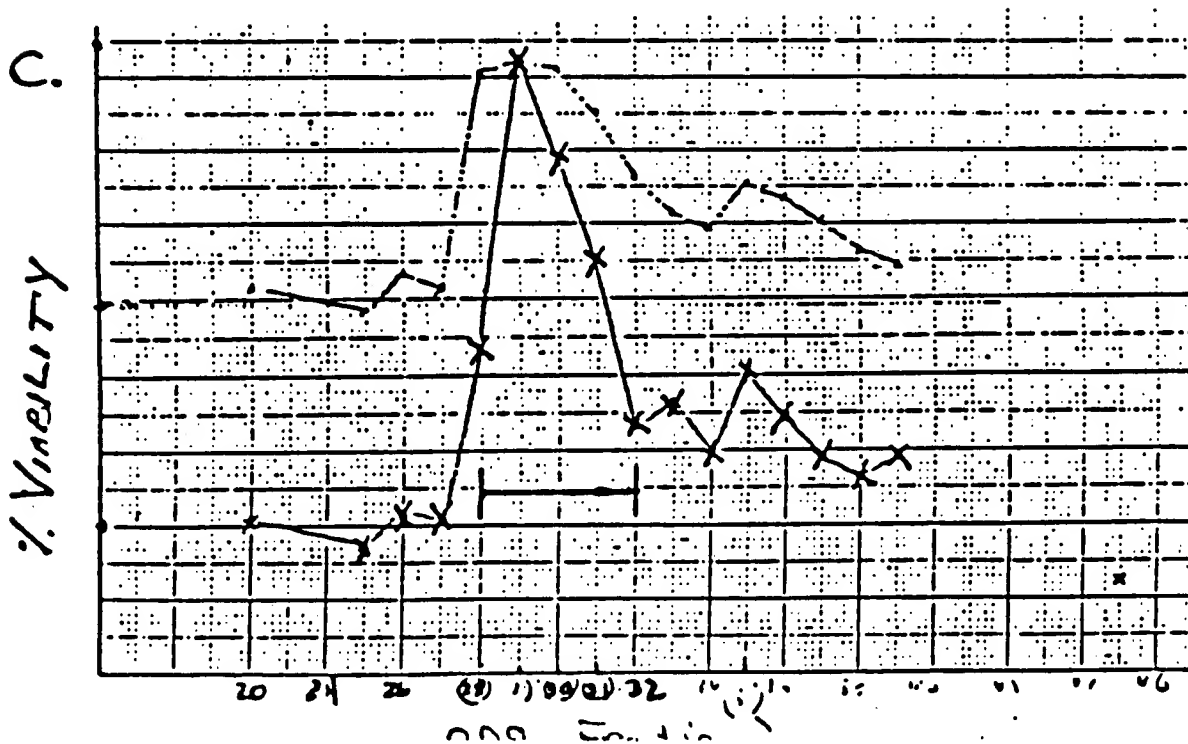
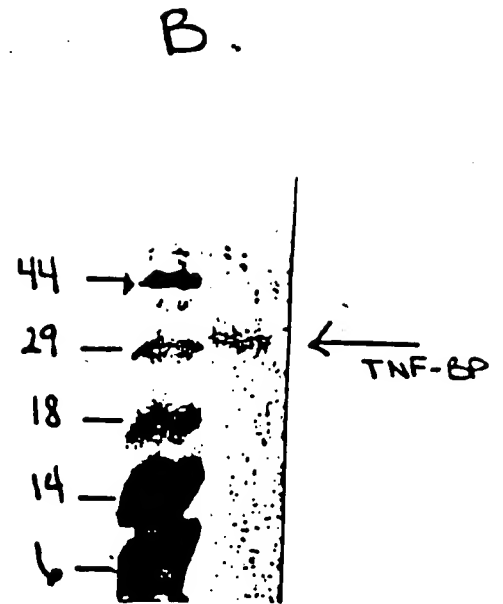
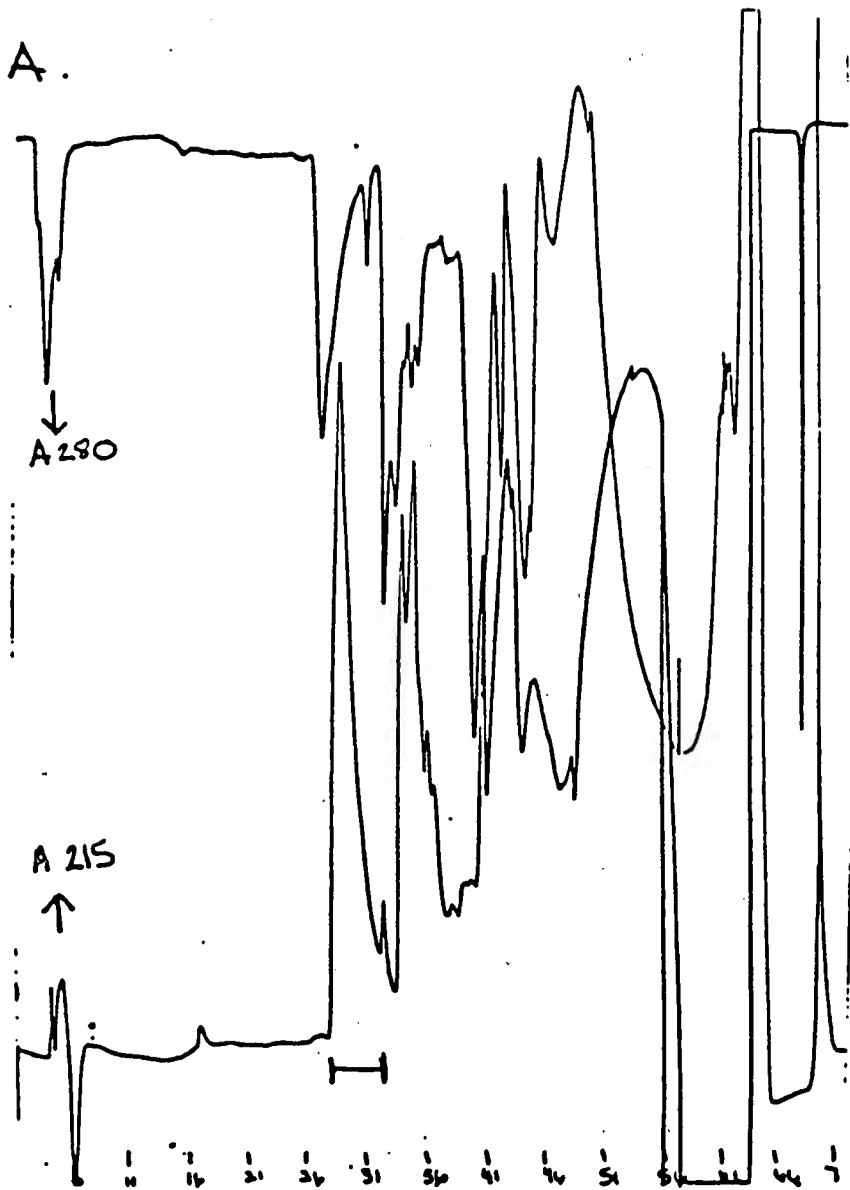


FIG. 9A

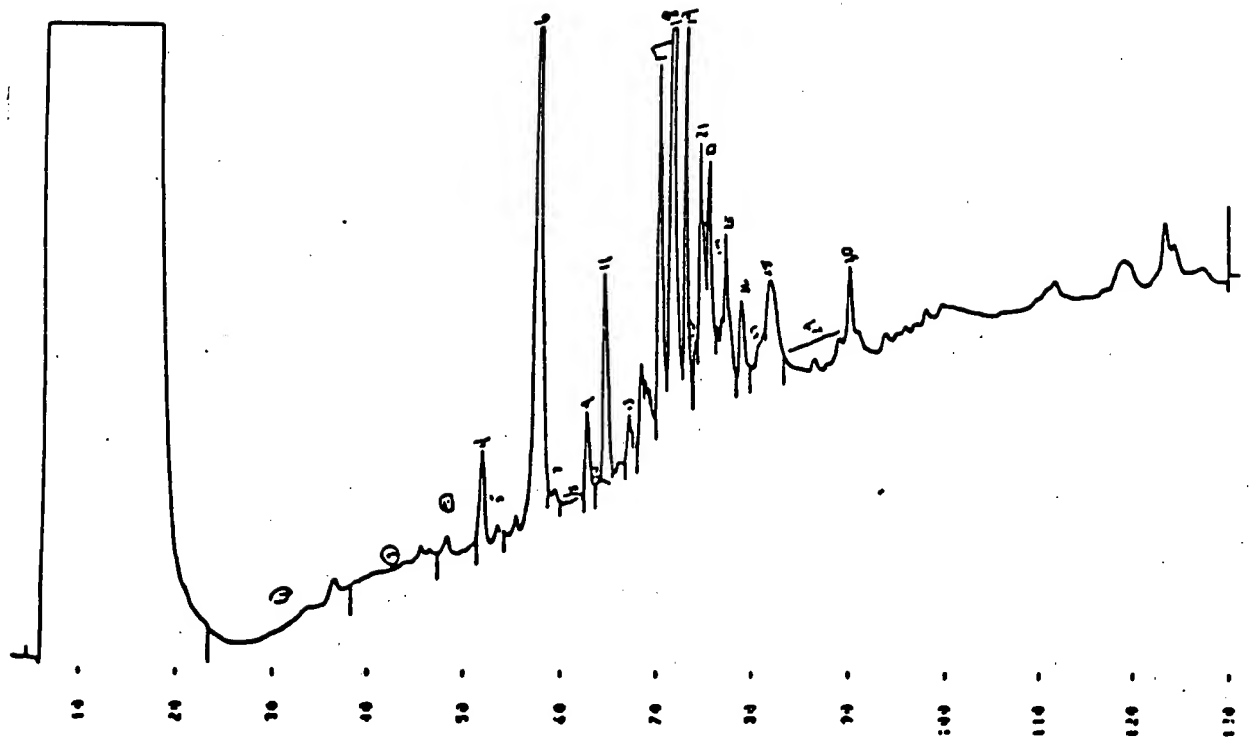
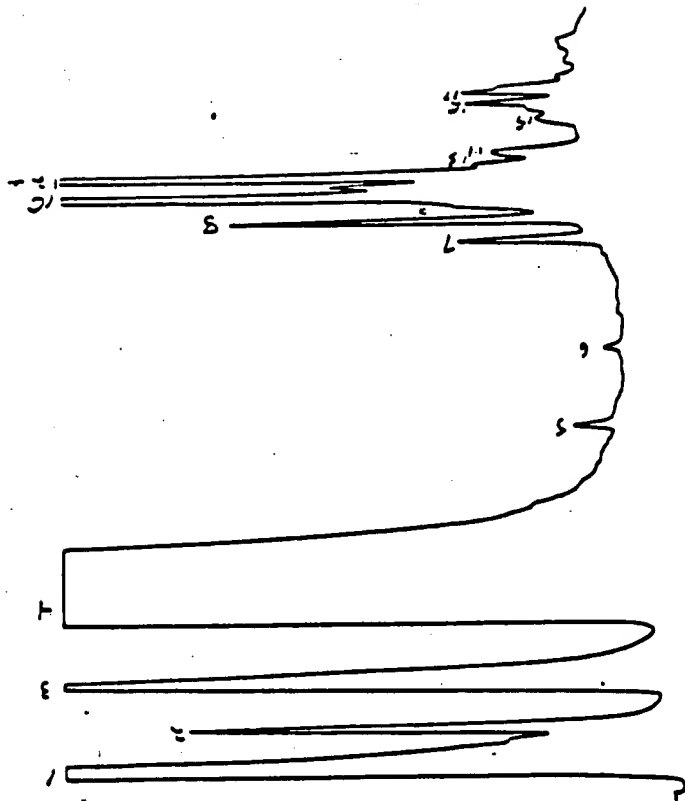
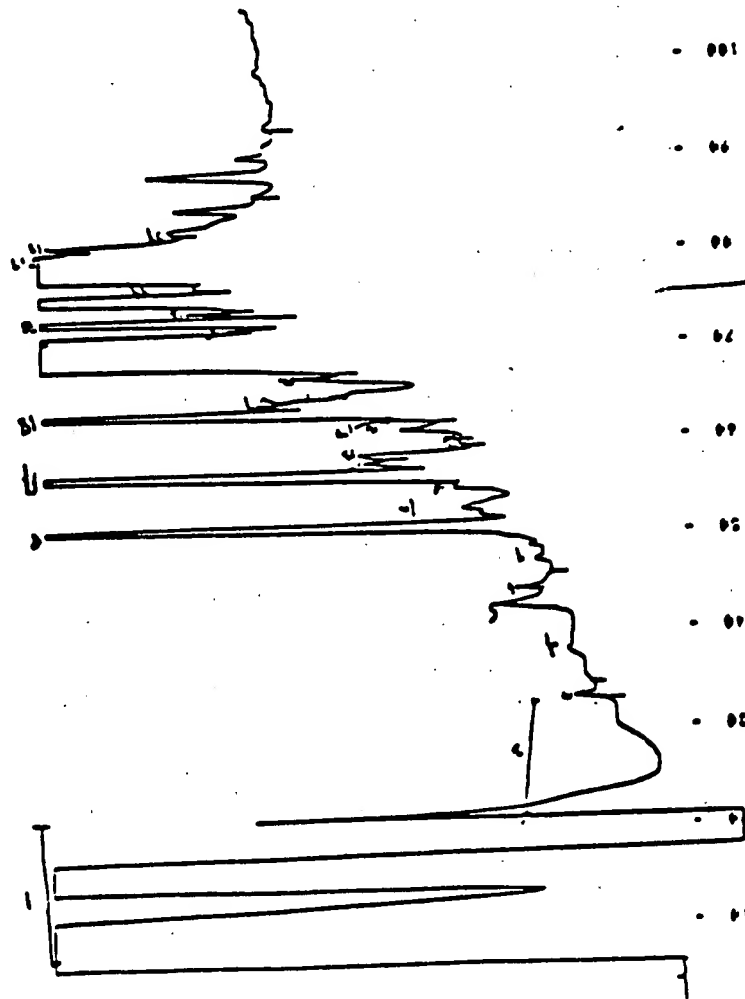


FIG 9B: ALKYLATED

* Lys-C digests of
TNF-BP

re-chromatograph
evens # 24, 26, 28, 32, 34



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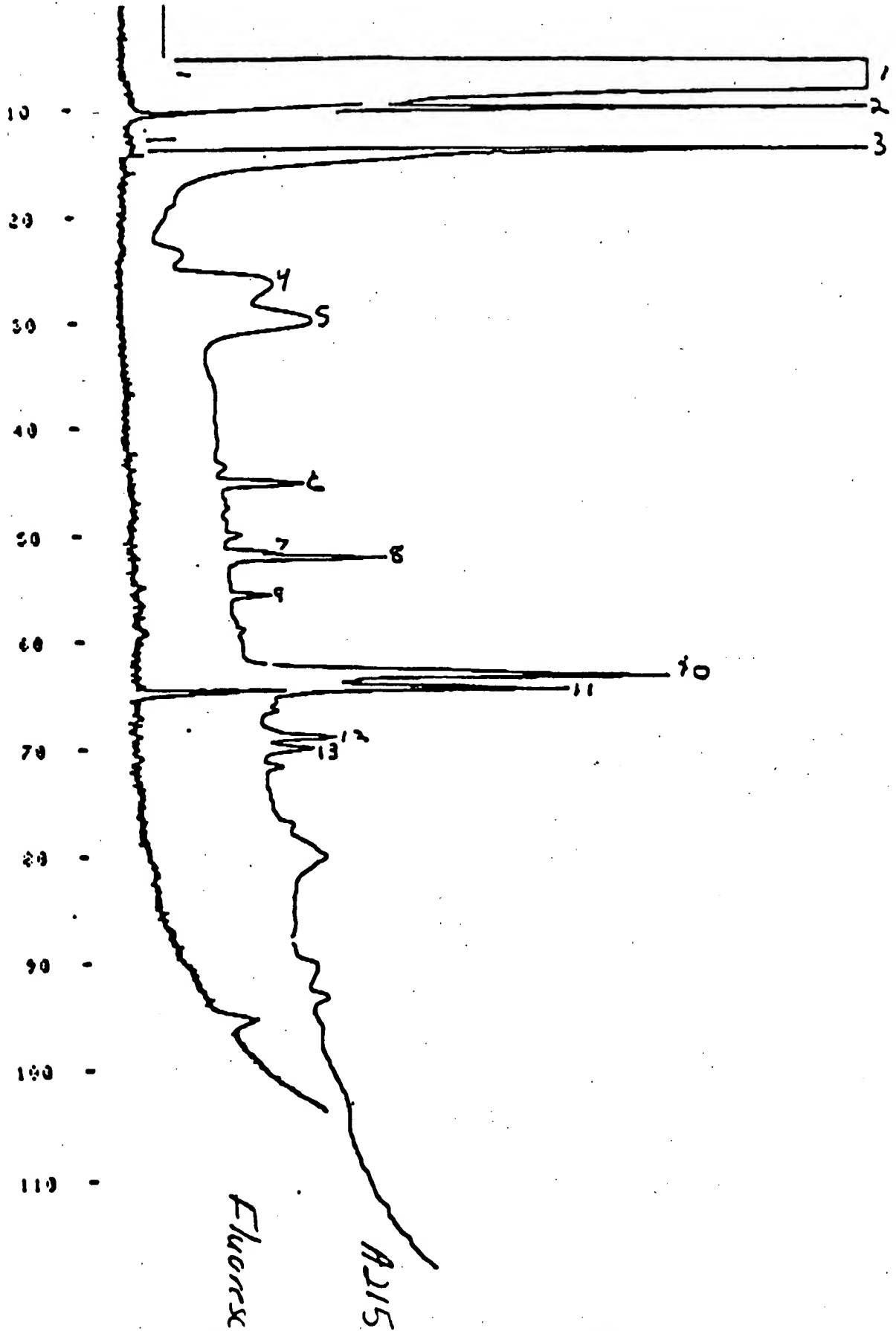
290

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2

FIG. 11A



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Fig. 11B

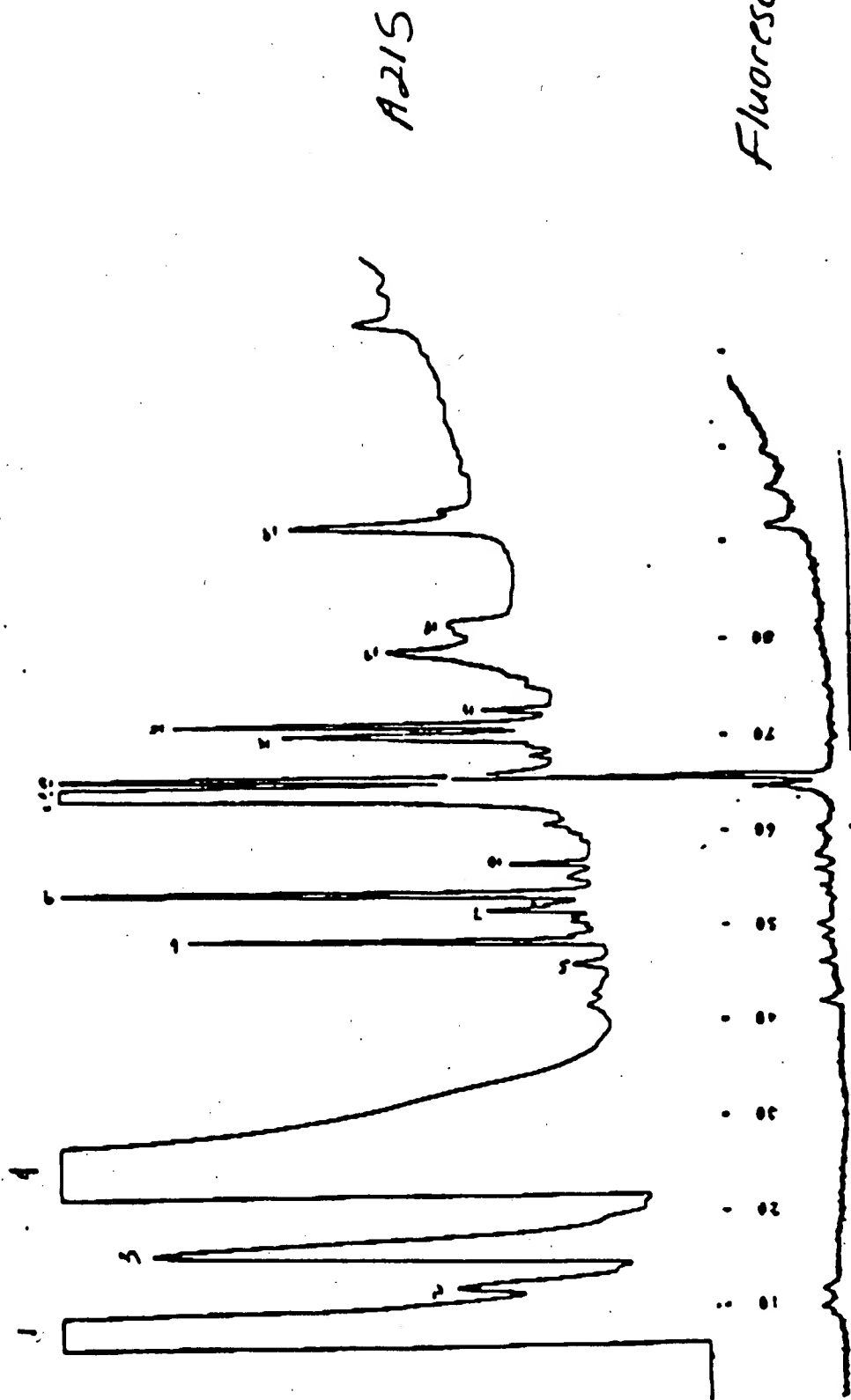


Figure 12

A. 1 10 20 30 40 50 60
 DSVCPCKYIPQNH SICCTKCKKGYLYHOCPPGQDTOC - - - SCSFTASEMLRLNCLSCS - - - K -
 B. (E) ZONTVCTCHAGTFLRENECVSC(L)MC(K)(E)(C)(L)(K)(E)
 C. (K)ENGOVEISSCTVDRTVCCREK(C)(V)(R)(H)(Y) - (O)
 (O)
 (K)(S)LECTKLCCLPOTEN - (S)(H)P(S)(A)
 (O)(A)

10 20 30 40 50 60 70
CATGCTGCA GGTGACTCT AGAGGATCTG GGUCCTACTA GCTTTGAGTT GAGGGAACAA AAATGAALAC
80 90 100 110 120 130 140
ACAGGACAAAC TAGAGAACAA TTAAGCATCA GATTGTATGC CCCAACTGTC TAAGTTTCAA GGAAGAAGTC
150 160 170 180 190 200 210
TAAACTTAGT GAGTGGCCTG GCCTGGGCGG AATGTTTCAC TGAGGAAGGA CTGGAUCCAG GGAAGTTTAA
220 230 240 250 260 270 280
GATCTGCTAC CCCTAAGCTT CCCATCCCTC CCTCTCTTGA TGGTGTCTCC TCTATCTGAT TCTTCCCCAG
289 298 307 316 325 334
GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCG TCA GGG GTT ATT GGA CTG GTC
Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val
343 352 361 370 379 388
CCT CAC CTA GGG GAC AGG GAG AAG AGA GAT AGT GTG TGT CCC CAA GCA AAA TAT
Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys Tyr
397 406 415 424 433 444
ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA G GTAGGGGCAA
Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys Ala
454 464 474 484 494 504 514
GTGGAACGG TGAATGCCCT CAGGTCTGGG GTGCTGCTTC TTTCTCTGCT TCTTCCAGTT GTTCTTCCCT
524 534 544 554 564 574 584
AACTTTGCTG TCTCTCTGG GUTGGGATT TCTCCCTCCC TCCTCTCCTA GAGACTTCAQ GGAATCGGCC
594 604 614 624 634 644 654
CTGCTCTTG TCCTAGCAT GGGGCTCCTT CCTTGTGTTT TCACCCGCAG CCAACTCTG CGGCCCCATT
664 673 682 691 700
CA CA GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACC GAC
Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp
709 718 727 736 745 754
TGC AGG GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AAG CAC
Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His
763 772 781 797 807 817
TGC CTC AGC TGC TCC AAA TGC CCA AAG GGTGAGTGT CACAGGCAGG AGAGTCAGGC
Cys Leu Ser Cys Ser Lys Cys Arg Lys
827 837 847 857 867 877 887
GGGTCTTGAQ TGGTGTGTGG GTGCCTGTCT ATGTGCAGGC TGGTGGGTOT GGGCAGGAAG GTGTGTGTTT
897 907 917 927 937 947 957
TGATGGAACA CTGATGGAT GTGAGTGTGT ATTACAGAGA CACACACTTA GGGGTATGTC AGHAAGGGA
967 977 987 997 1007 1016
TGCAGGAGAA GGAAGATGCA GAACTCATAC CCCATCTTCT CCCCACCA GAA ATG GAT CAG
Glu Met Gly Gln

1025
GTG GAG ATC
Val Glu Ile

FIG. 14

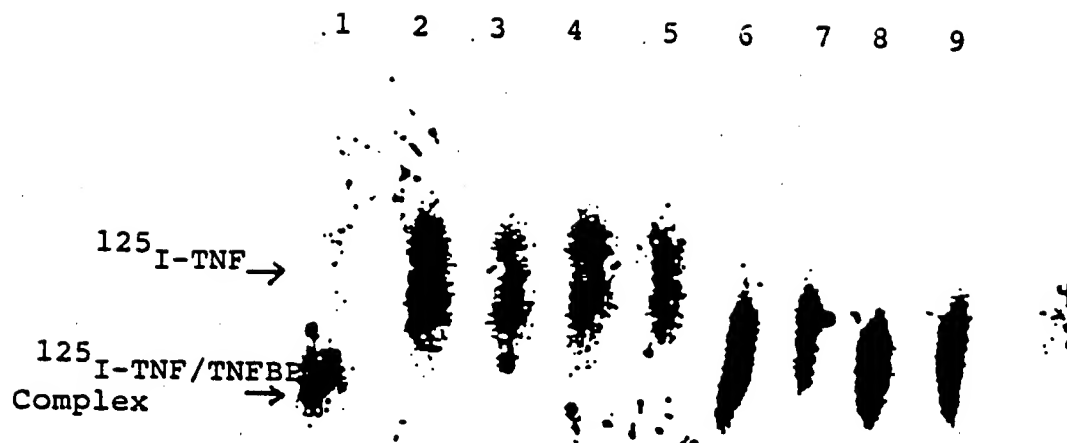
1 10 20 30 40 50 60 70 80
DSVCPQCKYINPOMNSICCTKCNKGTLYNOCPCPCGQOTDCRECESGSFTASENNLRNCLSCSKCKRKNMGQVEISSCTVORDT

90
VCGCRKN

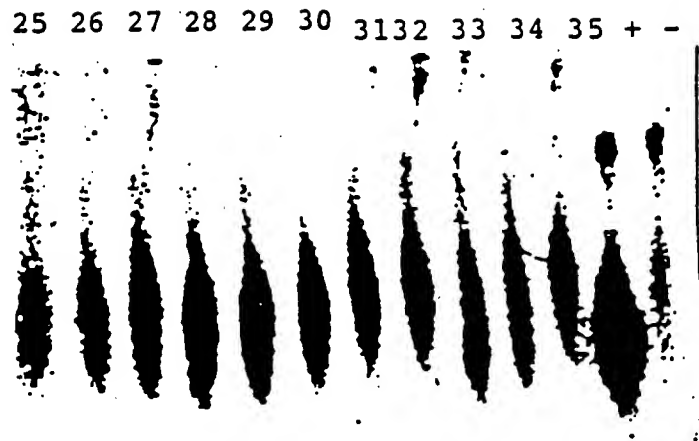
KONTVCTCHAGFFLRENECVSC

LECTKLCLPOIEN

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Lane 1 is a positive control. Purified TNF-BP complexed with $^{125}\text{I-TNF}$. Lane 2-5 are protein from the 24, 48, 72, and 96 hour incubations with PMA/PHA that did not bind to the TNF-affinity column. Lane 6-9 are the material from the same incubations that did bind to the TNF-affinity column.



Fractions 27, 28 and 29, 33 and 34 show TNF binding activity. + is as lane 1 of figure 15. - is 125I-TNF alone.

NO	PMA/PHA	
PMA/PHA	1hr	17hr

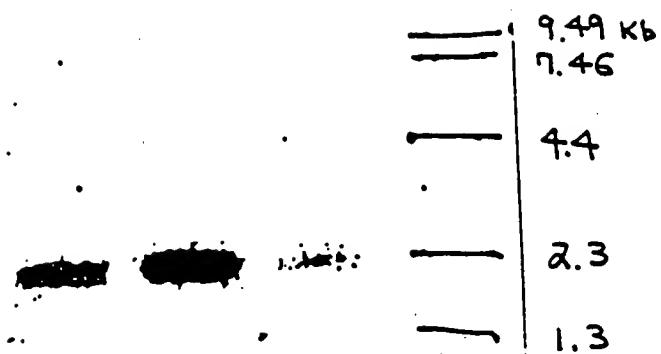


Fig 17



FIG 18

10
 Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr 20
 30
 Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp 40
 50
 Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu 60
 70
 Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp 80
 90
 Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu 100
 110
 Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu 120
 130
 Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val 140
 150
 Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu 160
 161
 Asn

FIG 19

Figure 20.

10 20 30 40 50 60 70
 SATCACTGGG ACCAGGCCGT GATCTCTATG CCCGAGTCTC AACCTCAAC TGTCACCCCA AGGCACTTGG

80 90 100 110 120 130 140
 GACGTCCTGG ACAGACCGAG TCCCGGGAAG CCCAGCACT GCCGCTGCCA CACTGCCCTG AGCCCAAATG

150 160 171 180 189 198
 GGGGAGTGAG AGGCCATAGC TGTCTGGC ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG
 MET Gly Leu Ser Thr Val Pro Asp Leu Leu

207 216 225 234 243 252
 CTG CCG CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT
 Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile

261 270 279 288 297 306
 GGA CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA GAT AGT GTG TGT CCC CAA
 Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln

315 324 333 342 351 360
 GGA AAA TAT ATC CAC CCT CAA AAT AAT TCG ATT TGC TGT ACC AAG TGC CAC AAA
 Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys

369 378 387 396 405 414
 GGA ACC TAC TTG TAC AAT GAC TGT CCA GGC CCG GGG CAG GAT ACG GAC TGC AGG
 Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg

423 432 441 450 459 468
 GAG TGT GAG AGC GGC TCC TTC ACC GCT TCA GAA AAC CAC CTC AGA CAC TGC CTC
 Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu

477 486 495 504 513 522
 AGC TGC TCC AAA TGC CGA AAG GAA ATG GGT CAG GTG GAG ATC TCT TCT TGC ACA
 Ser Cys Ser Lys Cys Arg Lys Glu MET Gly Gln Val Glu Ile Ser Ser Cys Thr

531 540 549 558 567 576
 GTG GAC CGG GAC ACC GTG TGT GGC TGC AGG AAG AAC CAG TAC CGG CAT TAT TGG
 Val Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr Trp

585 594 603 612 621 630
 AGT GAA AAC CTT TTC CAG TGC TTC AAT TGC AGC CTC TGC CTC AAT GGG ACC GTG
 Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val

639 648 657 666 675 684
 CAC CTC TCC TGC CAG GAG AAA CAG AAC ACC GTG TGC ACC TGC CAT GCA GGT TTC
 His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe

Fig 21

693			702			711			720			729			738		
TTT	CTA	AGA	GAA	AAC	GAG	TGT	GTC	TCC	TGT	AGT	AAC	TGT	AAG	AAA	AGC	CTG	GAG
Phe	Leu	Arg	Glu	Asn	Glu	Cys	Val	Ser	Cys	Ser	Asn	Cys	Lys	Lys	Ser	Leu	Glu
747			756			765			774			783			792		
TGC	ACG	AAG	TTG	TGC	CTA	CCC	CAG	ATT	GAG	AAT	GTT	AAG	GGC	ACT	GAG	GAC	TCA
Cys	Thr	Lys	Leu	Cys	Leu	Pro	Gln	Ile	Glu	Asn	Val	Lys	Gly	Thr	Glu	Asp	Ser
801			810			819			828			837			846		
GGC	ACC	ACA	GTG	CTG	TTG	CCC	CTG	GTC	ATT	TTC	TTT	GGT	CTT	TGC	CTT	TTA	TCC
Gly	Thr	Thr	Val	Leu	Leu	Pro	Leu	Val	Ile	Phe	Phe	Gly	Leu	Cys	Leu	Leu	Ser
855			864			873			882			891			900		
CTC	CTC	TTC	ATT	GGT	TTA	ATG	TAT	CGC	TAC	CAA	CGG	TGG	AAG	TCC	AAG	CTC	TAC
Leu	Leu	Phe	Ile	Gly	Leu	MET	Tyr	Arg	Tyr	Gln	Arg	Trp	Lys	Ser	Lys	Leu	Tyr
909			918			927			936			945			954		
TCC	ATT	GTT	TGT	GGG	AAA	TGG	ACA	CCT	GAA	AAA	GAG	GGG	GAG	CTT	GAA	GGG	ACT
Ser	Ile	Val	Cys	Gly	Lys	Ser	Thr	Pro	Glu	Lys	Glu	Gly	Glu	Leu	Glu	Gly	Thr
963			972			981			990			999			1008		
ACT	ACT	AAG	CCC	CTG	GCC	CCA	AAC	CCA	AGC	TTC	AGT	CCC	ACT	CCA	GGC	TTC	ACC
Thr	Thr	Lys	Pro	Leu	Ala	Pro	Asn	Pro	Ser	Phe	Ser	Pro	Thr	Pro	Gly	Phe	Thr
1017			1026			1035			1044			1053			1062		
CCC	ACC	CTG	GGC	TTC	AGT	CCC	GTC	CCC	AGT	TCC	ACC	TTC	ACC	TCC	AGC	TCC	ACC
Pro	Thr	Leu	Gly	Phe	Ser	Pro	Val	Pro	Ser	Ser	Thr	Phe	Thr	Ser	Ser	Ser	Thr
1071			1080			1089			1098			1107			1116		
TAT	ACC	CCC	GGT	GAC	TGT	CCC	AAC	TTT	GCG	GCT	CCC	CGC	AGA	GAG	GTG	GCA	CCA
Tyr	Thr	Pro	Gly	Asp	Cys	Pro	Asn	Phe	Ala	Ala	Pro	Arg	Arg	Glu	Val	Ala	Pro
1125			1134			1143			1152			1161			1170		
CCC	TAT	CAG	GGG	GCT	GAC	CCC	ATC	CTT	GCG	ACA	GCC	CTC	GCC	TCC	GAC	CCC	ATC
Pro	Tyr	Gln	Gly	Ala	Asp	Pro	Ile	Leu	Ala	Thr	Ala	Leu	Ala	Ser	Asp	Pro	Ile
1179			1188			1197			1206			1215			1224		
CCC	AAC	CCC	CTT	CAG	AAG	TGG	GAG	GAC	AGC	GCC	CAC	AAG	CCA	CAG	AGC	CTA	GAC
Pro	Asn	Pro	Leu	Gln	Lys	Trp	Glu	Asp	Ser	Ala	His	Lys	Pro	Gln	Ser	Leu	Asp
1233			1242			1251			1260			1269			1278		
ACT	GAT	GAC	CCC	GCG	ACG	CTG	TAC	GCC	GTG	GTG	GAG	AAC	GTG	CCC	CCG	TTG	CGC
Thr	Asp	Asp	Pro	Ala	Thr	Leu	Tyr	Ala	Val	Val	Glu	Asn	Val	Pro	Pro	Leu	Arg
1287			1296			1305			1314			1323			1332		
TGG	AAG	GAA	TTC	GTG	CGG	CGC	CTA	GGG	CTG	AGC	GAC	CAC	GAG	ATC	GAT	CGG	CTG
Trp	Lys	Glu	Phe	Val	Arg	Arg	Leu	Gly	Leu	Ser	Asp	His	Glu	Ile	Asp	Arg	Leu

1341	1350	1359	1368	1377	1386
GAG CTG CAG AAC GGG CGC TGC CTG CGC GAG GCG CAA TAC AGC ATG CTG GCG ACC					
Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln Tyr Ser MET Leu Ala Thr					
1395	1404	1413	1422	1431	1440
TGG AGG CCG CGC ACG CCG CGG CGC GAG GCC ACG CTG GAG CTG CTG GGA CCG GTG					
Trp Arg Arg Arg Thr Pro Arg Arg Glu Ala Thr Leu Glu Leu Leu Gly Arg Val					
1449	1458	1467	1476	1485	1494
CTC CGC GAC ATG GAC CTG CTG GGC TGC CTG GAG GAC ATC GAG GAG GCG CTT TGC					
Leu Arg Asp MET Asp Leu Leu Gly Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys					
1503	1512	1521	1530	1546	1556
GGC CCC GCC GCC CTC CCG CCC GCG CCC AGT CTT CTC AGA TGA					
Gly Pro Ala Ala Leu Pro Pro Ala Pro Ser Leu Leu Arg					
1566	1576	1586	1596	1606	1626
CTCTAAGBAC CGTCCTGCGA GATCGCCTTC CAACCCCACT TTTTCTGGA AAGGAGGGGT CCTGCAGGGG					
1636	1646	1656	1666	1676	1696
CAAGCAGGAG CTAGCAGCCG CCTACTTGGT GCTAACCCTT CGATGTACAT AGCTTTTCTC AGCTGCCTGC					
1706	1716	1726	1736	1746	1766
GCGCCGCCGA CAGTCAGCGC TGTGCGCGCG GAGAGAGGTG CGCCGTGGGC TCAAGAGCCT GAGTGGGTGG					
1776	1786	1796	1806	1816	1836
TTTGCAGGGA TGAGGGACGC TATGCCTCAT GCCCGTTTTG GGTGTCCTCA CCAGCAAGGC TGCTCGGGGG					
1846	1856	1866	1876	1886	1906
CCCCTGGTTC GTCCCTGAGC CTTTTTCACA GTGCATAAGC AGTTTTTTTT GTTTTTGTTT TGTTTTGT					
1916	1926	1936	1946	1956	1976
TGTTTTTAAA TCAATCATGT TACACTAATA GAAACTTGGC ACTCCTGTGC CCTCTGCCTG GACAAGCACA					
1986	1996	2006	2016	2026	2046
TAGCAAGCTG AACTGTCCTA AGGCAGGGGC GAGCACGGAA CAATGGGGCC TTCAGCTGGA GCTGTGGACT					
2056	2066	2076	2086		
TTTGTACATA CACTAAAATT CTGAAGTTAA AGCTCAAAAA AA					

FIG. 22

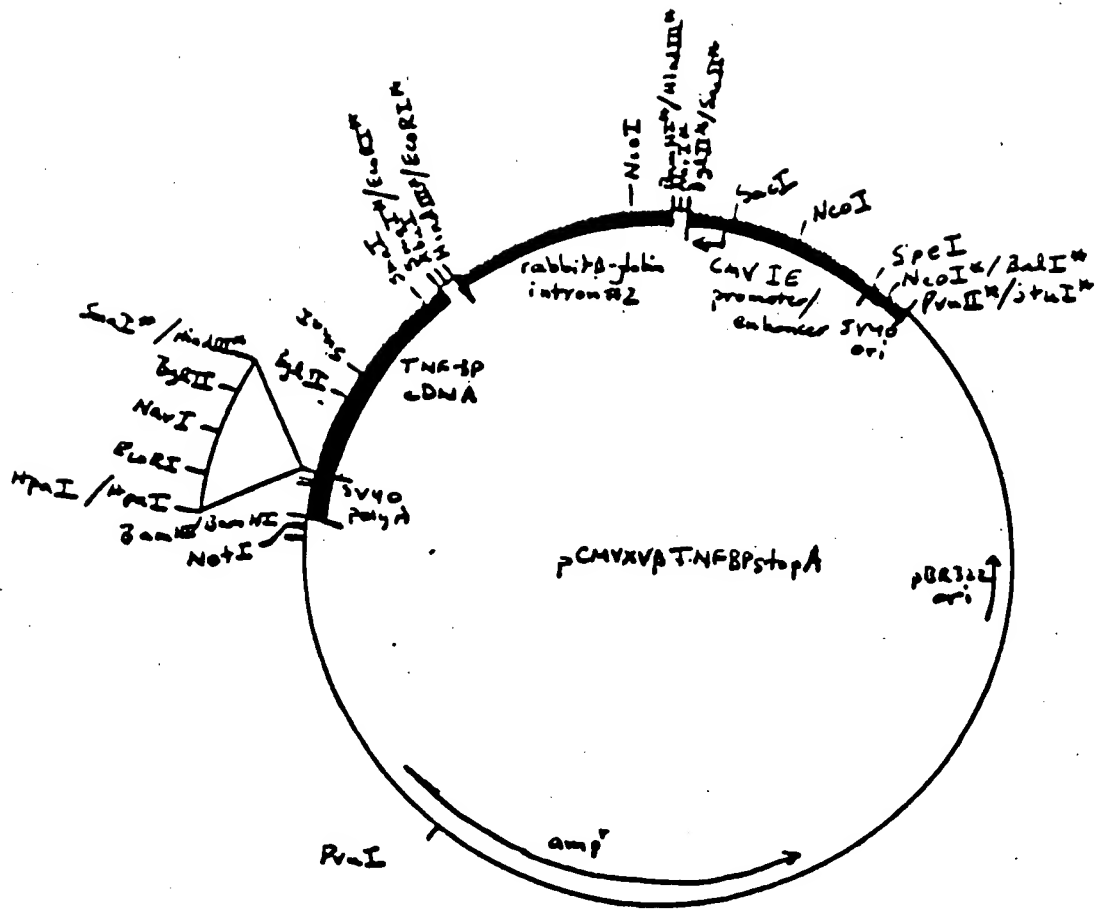
GA ATT CCA CAA CGG TTT CCC TCT AGA AAT AAT TTT GTT TAA CTT TAA GAA GGA GAT ATA CAT

Start gene 10 protein sequence

ATG GCT AGC ATG ACT GGT GGA CAG CAA ATG GGT ACG GAT CCG ATC TTG GAG GAT GAT TAA
Met Ala Ser Met Thr Gly Gly Gln Met Gly Thr Asp Pro Ile Leu Glu Asp Asp Stop
Translational coupler

ATG GAC AGC GTT TGC CCC
Met Asp Ser Val Cys Pro
Start TNF inhibitor Sequence

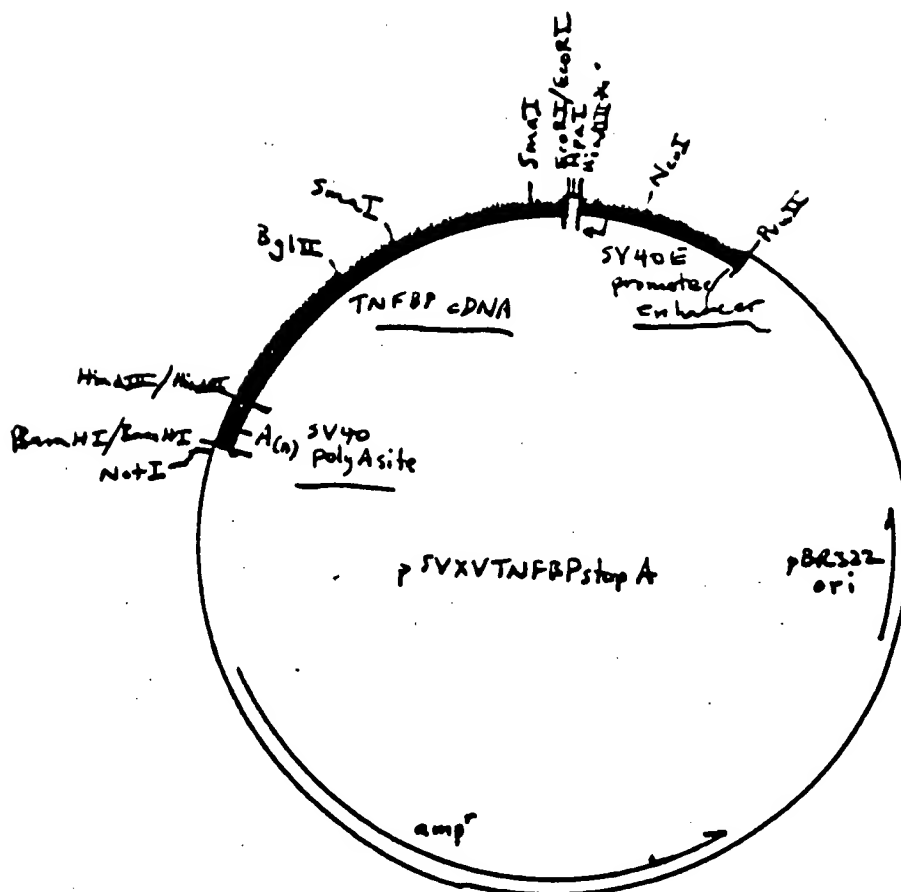
Fig. 23



* indicates restriction site no longer exists.

Fig. 24

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x - restriction site no longer exists.

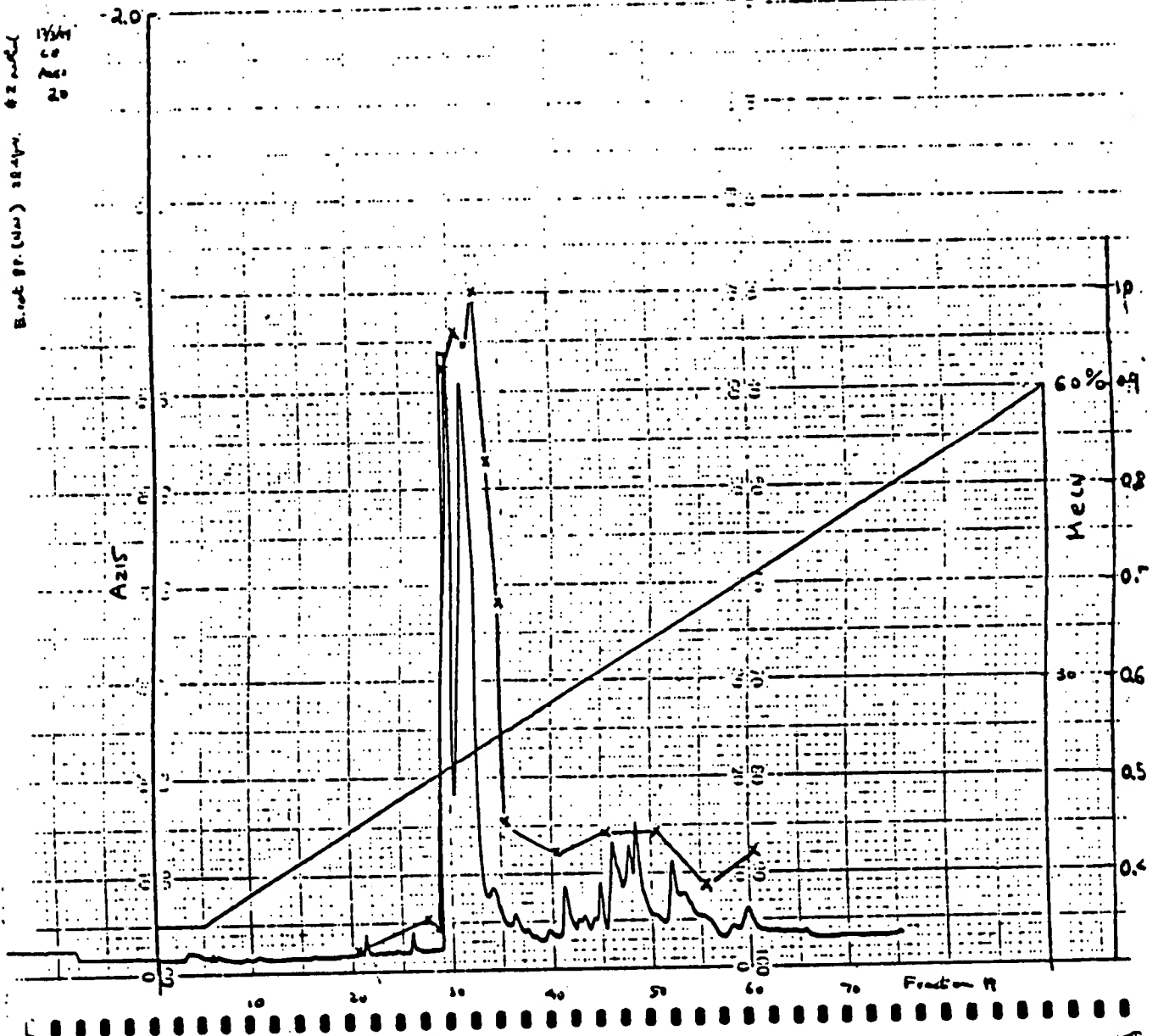


Figure 25

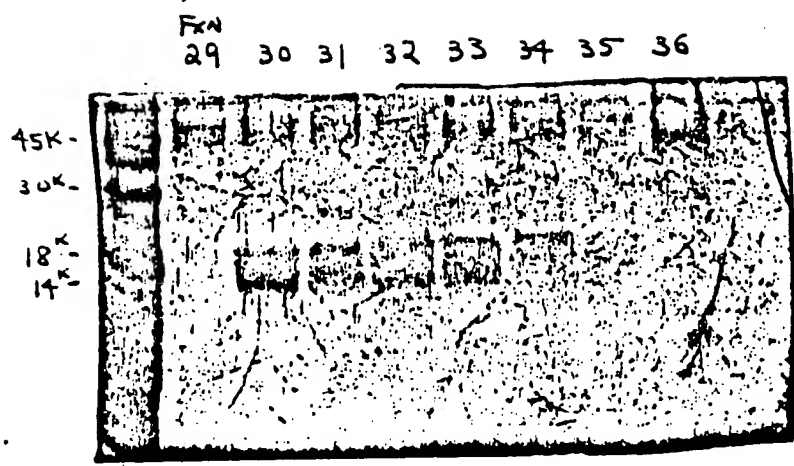


Figure 26

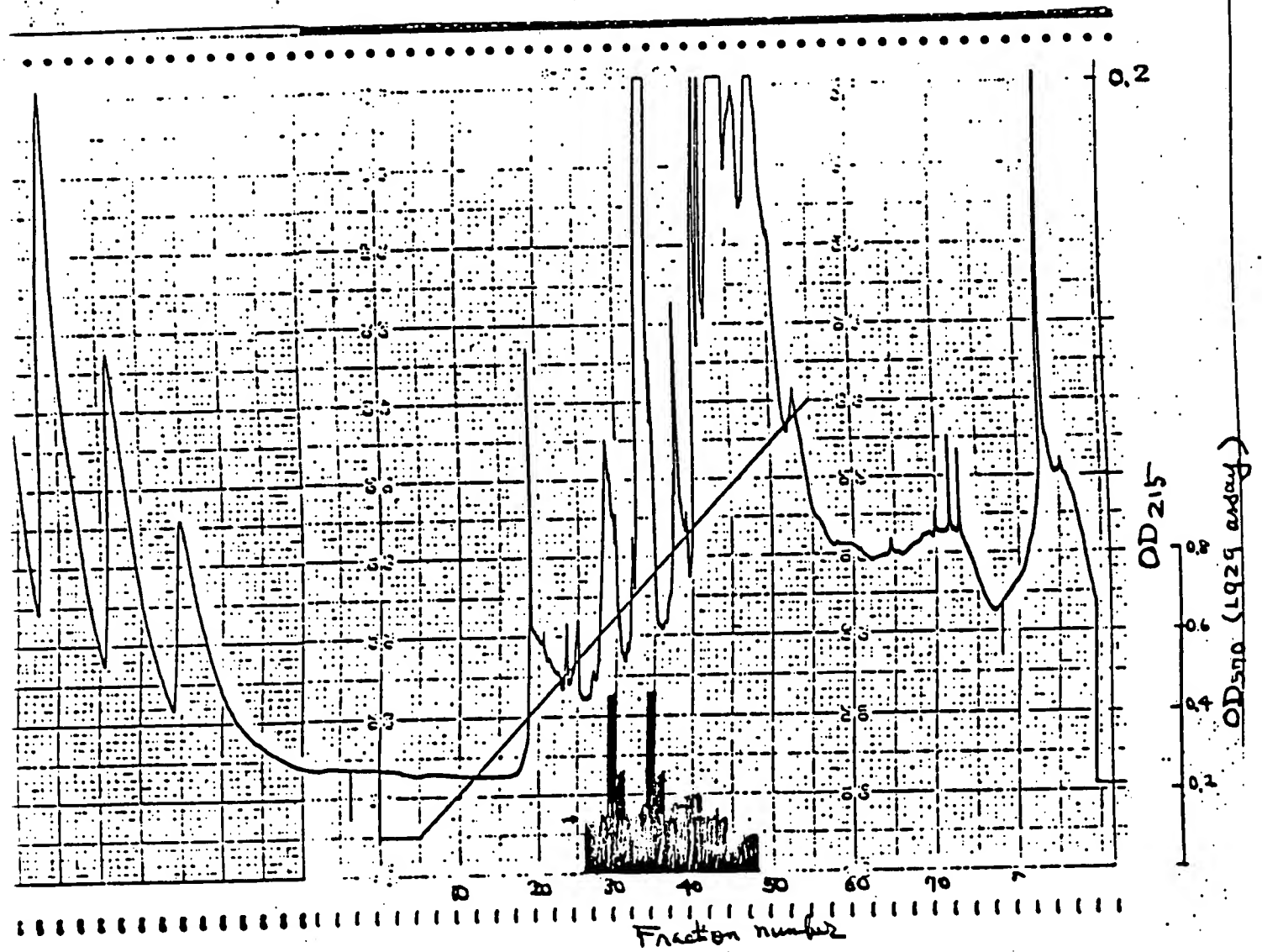


Fig. 27

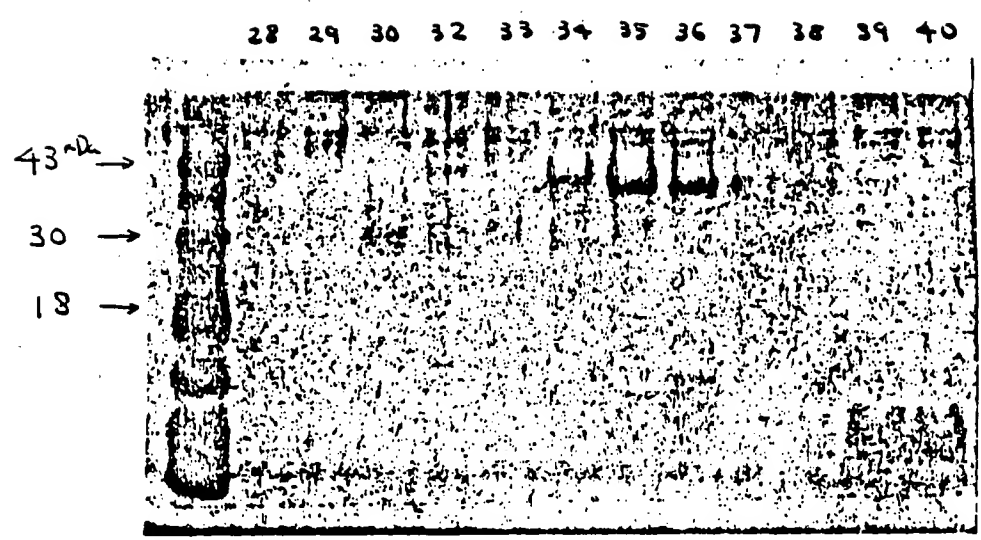


Fig. 28

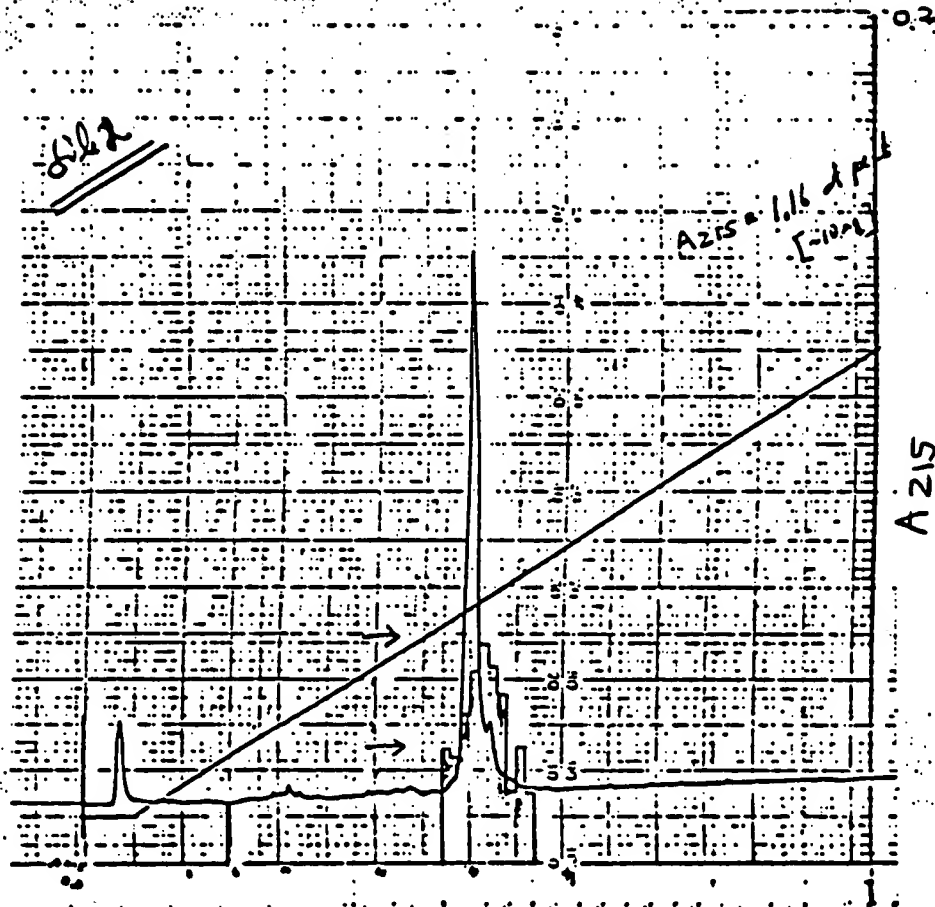
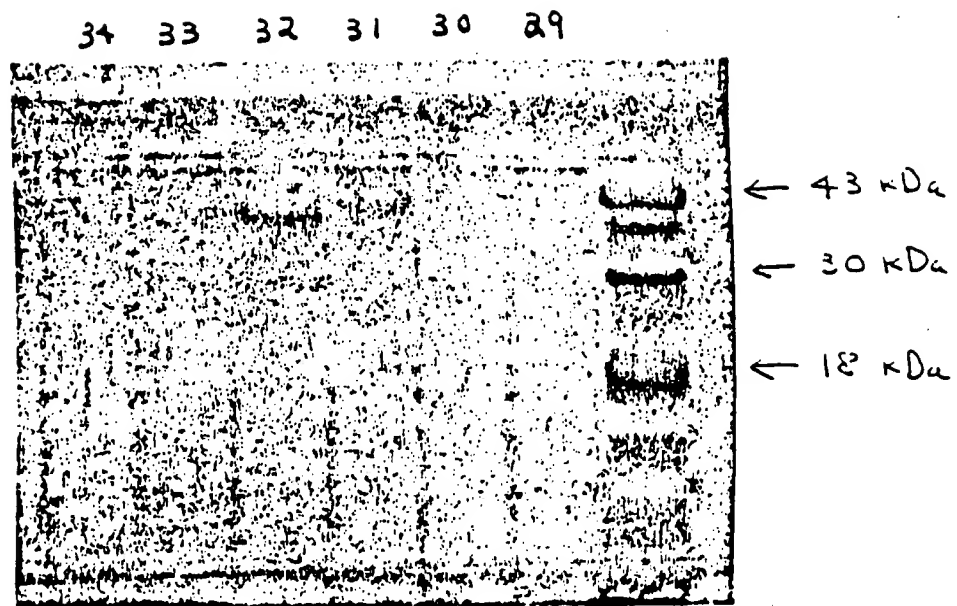


Fig. 29



U937-derived TNF-INH1 (30 kDa)

()-()-Val-()-Pro-Gln-GLY-Lys-Tyr-Ile-His-Pro-Gln-
()-Asn-()-Ile

U939-derived TNF-INH2 (40 kDa)

Leu-Pro-Ala-Gln-Val-Ala-Phe-Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-
Ser-Thr-Cys-Arg-Leu-Arg-Glu-Tyr-Tyr-Asp-Gln-Thr-Ala-Gln-Met-
Cys-Cys-Ser-Lys-Cys-

Urine-derived TNF-INH2 (40 kDa)

Ala-Gln-Val-Ala-Phe-Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr-
Cys-()-Leu-()-Glu

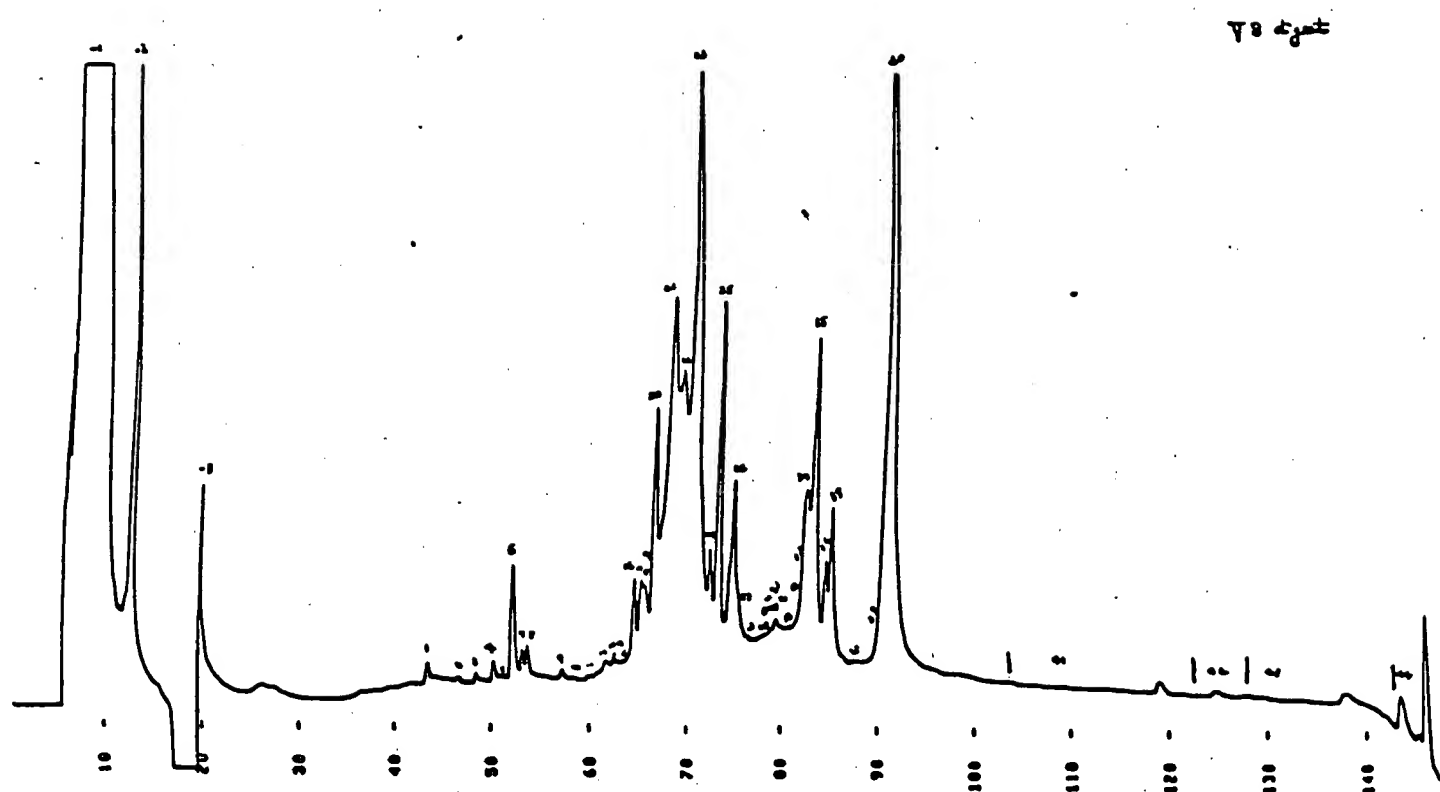


Figure 32

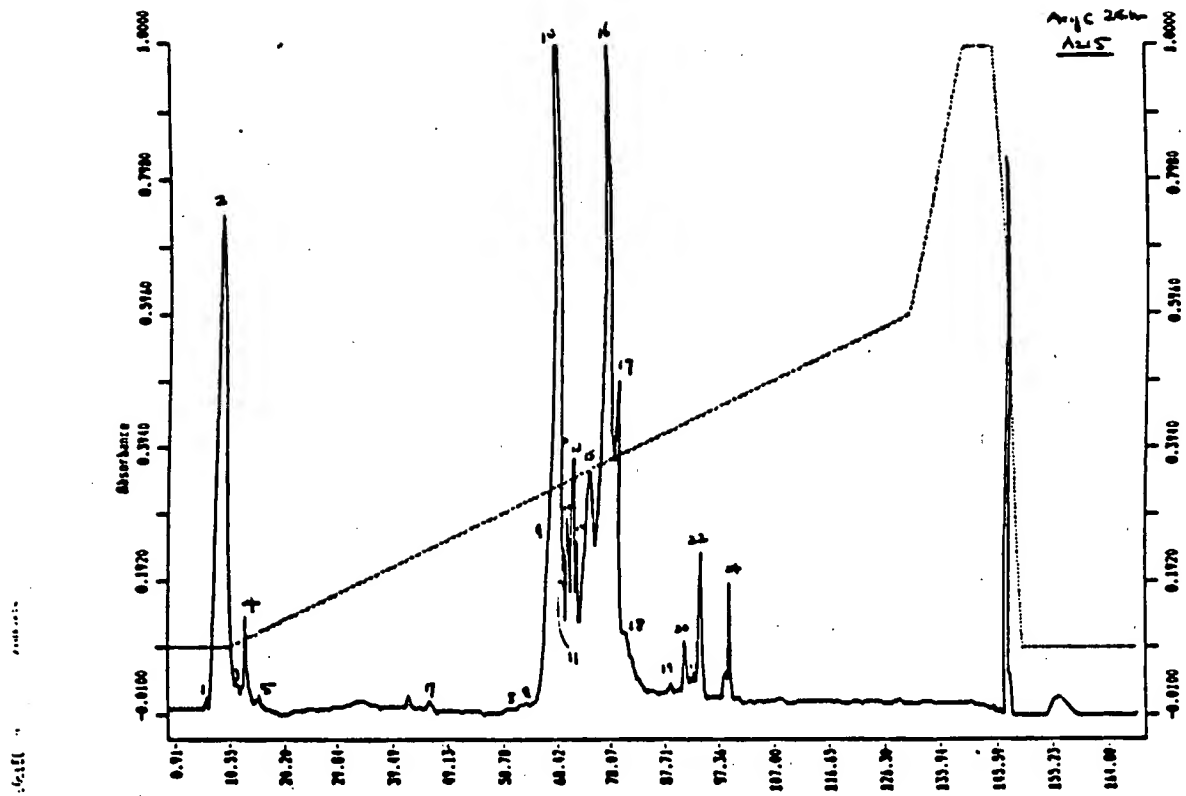


Figure 33

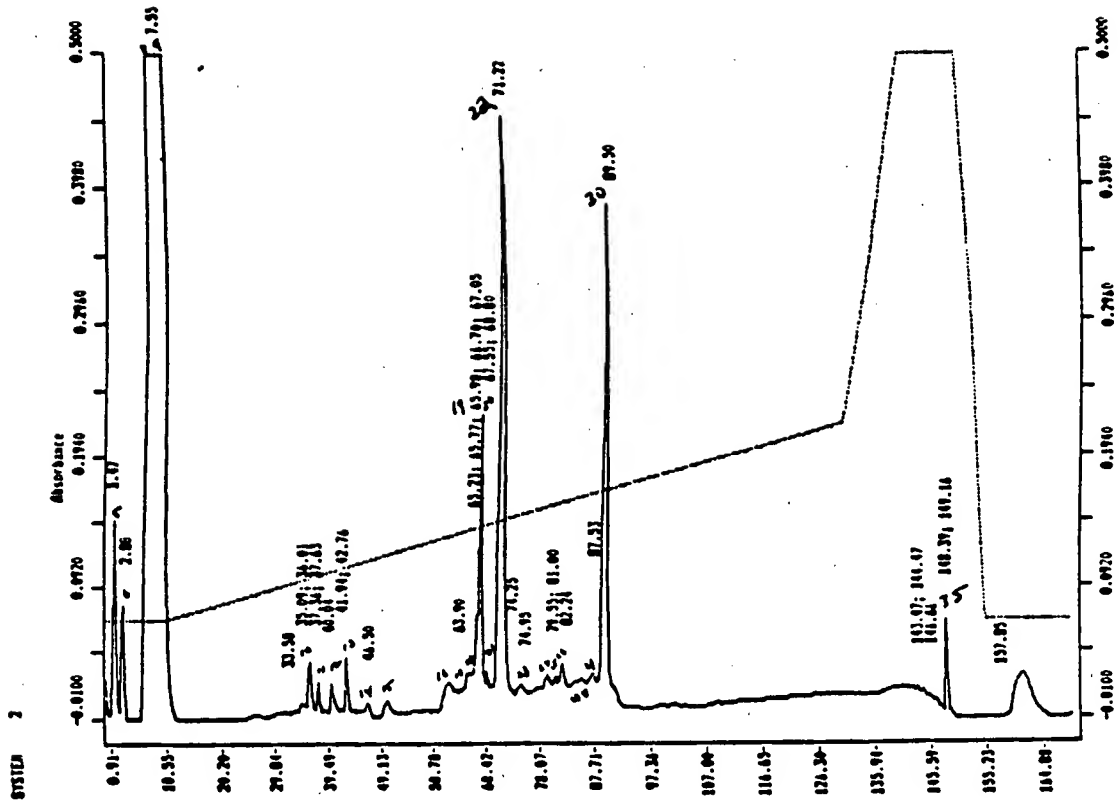


Figure 34

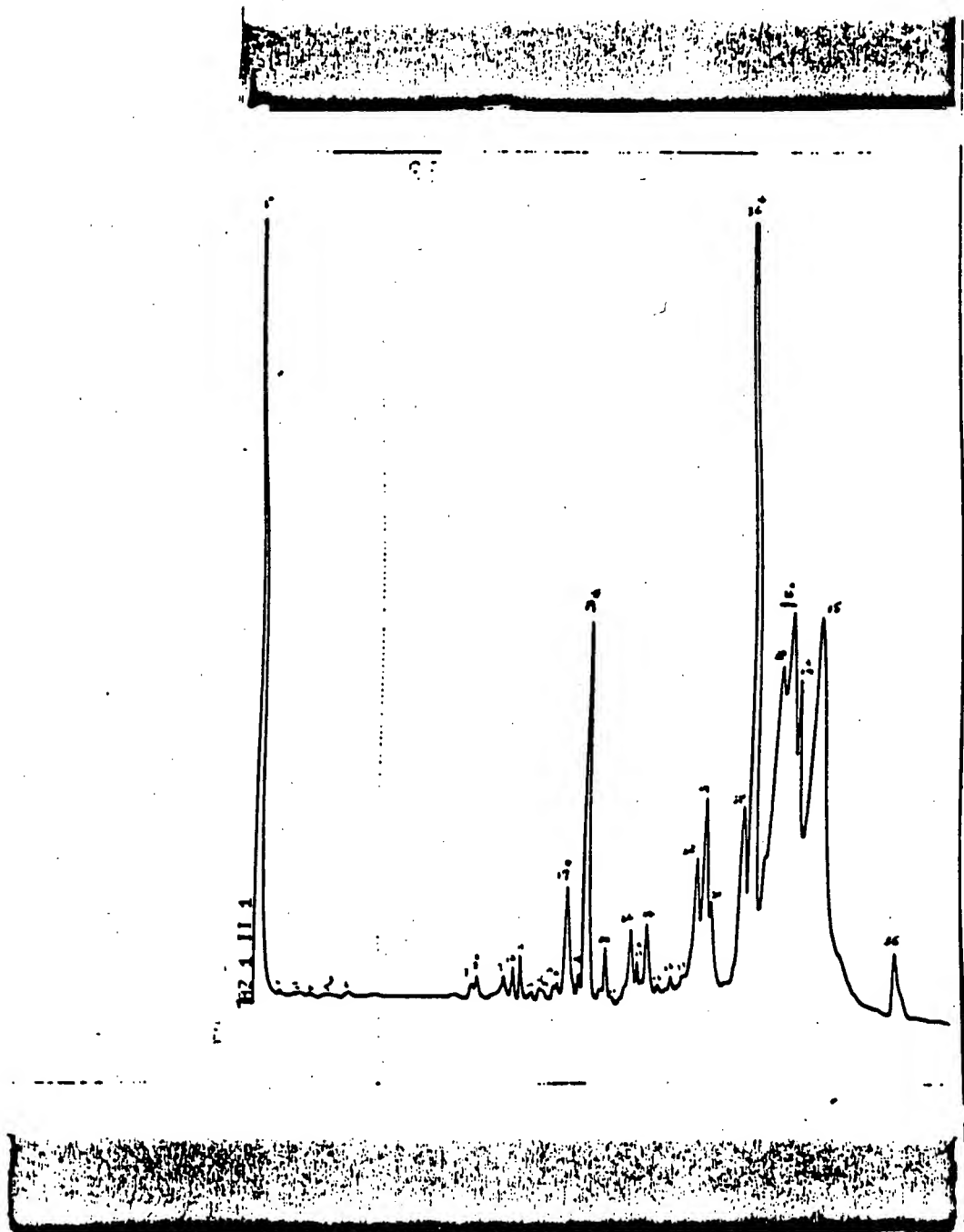


Figure 35

1 10 20 30 40 50 60 70 80
I P A Q V A F T P V A P E P G S T C R L R E V Y D O T A Q H C C S K C S P G Q H A K V F C T K T S O T V C D S C E D S T Y T Q L _ N _ V P E C L S C G S R C S S

NT

V25

V34.35

V37

V6

R12

R16

R4

R16 T30

R16 T30 V9

R16 T30 V4

R4

90 100 110 120 130 140 150
O Q V E _ _ A C T R E Q H R I C T C R P G W Y C A L S K Q E C R L C A P L R K C R P G F G V A R P G T E T S D V V C K P C A P G T F S _ T T S (T/D)(P)(C/R/P)

V23

V20

R4

R14

R10

R16 T13

R10 C19

R10 C17

R10

08/484337

Figure 37

5' - $\overline{\text{CCG}}$
Pro

57	64			73			82			91			100				
<u>GAG</u> Glu	<u>CCC</u> Pro	<u>GCG</u> Gly	<u>AGC</u> Ser	<u>ACA</u> Thr	<u>TGC</u> Cys	<u>CGG</u> Arg	<u>CTC</u> Leu	<u>AGA</u> Arg	<u>GAA</u> Glu	<u>TAC</u> Tyr	<u>TAT</u> Tyr	<u>GAC</u> Asp	<u>CAG</u> Gln	<u>ACR</u> Thr	<u>GCW</u> Ala	<u>CAR</u> Gln	<u>ATG</u> MET
109	118			127			136			145			154				
<u>TGC</u> Cys	<u>TGC</u> Cys	<u>AGC</u> Ser	<u>AAG</u> Lys	<u>TGC</u> Cys	<u>TGC</u> Ser	<u>CCG</u> Pro	<u>GGC</u> Gly	<u>CAA</u> Gln	<u>CAT</u> His	<u>GCA</u> Ala	<u>AAA</u> Lys	<u>GTC</u> Val	<u>TTC</u> Phe	<u>TGT</u> Cys	<u>ACC</u> Thr	<u>AAG</u> Lys	<u>ACC</u> Thr
163	172			181			190			199			208				
<u>TCC</u> Ser	<u>GAC</u> Asp	<u>ACC</u> Thr	<u>GTG</u> Val	<u>TGT</u> Cys	<u>GAC</u> Asp	<u>TCC</u> Ser	<u>TGT</u> Cys	<u>GAG</u> Glu	<u>GAC</u> Asp	<u>AGC</u> Ser	<u>ACA</u> Thr	<u>TAC</u> Tyr	<u>ACC</u> Thr	<u>CAG</u> Gln	<u>CTC</u> Leu	<u>TGG</u> Trp	<u>AAC</u> Asn
217	226			235			244			253			262				
<u>TGG</u> Trp	<u>GTT</u> Val	<u>CCC</u> Pro	<u>GAG</u> Glu	<u>TGC</u> Cys	<u>TTG</u> Leu	<u>AGC</u> Ser	<u>TGT</u> Cys	<u>GGC</u> Gly	<u>TCC</u> Ser	<u>CGC</u> Arg	<u>TGT</u> Cys	<u>AGC</u> Ser	<u>TCT</u> Ser	<u>GAC</u> Asp	<u>CAG</u> Gln	<u>GTG</u> Val	<u>GAA</u> Glu
271	280			289			298			307			316				
<u>ACT</u> Thr	<u>CAA</u> Gln	<u>GCC</u> Ala	<u>TGC</u> Cys	<u>ACT</u> Thr	<u>CGG</u> Arg	<u>GAA</u> Glu	<u>CAG</u> Gln	<u>AAC</u> Asn	<u>CGC</u> Arg	<u>ATC</u> Ile	<u>TGC</u> Cys	<u>ACC</u> Thr	<u>TGC</u> Cys	<u>AGG</u> Arg	<u>CCC</u> Pro	<u>GGC</u> Gly	<u>TGG</u> Trp

325

$\overline{\text{TAY}}$ Tyr	$\overline{\text{TGC}}$ Cys	- 3'

Figure 38

Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln MET Cys Cys
Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser
Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His
Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Arg Asp Ala
Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET Ala Pro Gly Ala Val
His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr
Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET Gly
Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp

10 30 40 50 70
 DAATTCGGCG CAGCGG TGGAGAGAG GCGCTGGCT GCGAGGCGC GAGGGGGA GGGCAGGGGG

60	70	101	110	119
CAACCGGACC	CCGCCCGCAC	CC ATG GCG CCC GTC GCG GTC TGG GCG GCG CTG GCC		
		MET Ala Pro Val Ala Val Trp Ala Ala Leu Ala		
128	137	146	155	164
GTC GGA CTG GAG CTC TGG GCT GCG GCG CAC GCG TTG CCC GCG CAG GTG GCA TTT				
Val Gly Leu Glu Leu Trp Ala Ala Ala His Ala Leu Pro Ala Gln Val Ala Phe				
182	191	200	209	218
ACA CCC TAC GCG CCG GAG CCC GGG AGC ACA TGC CCG CTC AGA GAA TAC TAT GAC				
Thr Pro Tyr Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp				
236	245	254	263	272
CAG ACA GCT CAG ATG TGC TGC AGC AAG TGC TCG CCG GCG CAA CAT GCA AAA GTC				
Gln Thr Ala MET Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val				
290	299	308	317	326
TTC TGT ACC AAG ACC TCG GAC ACC GTG TGT GAC TCC TGT GAG GAC AGC ACA TAC				
Phe Cys Thr Lys Thr Ser Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr				
344	353	362	371	380
ACC CAG CTC TGG AAC TGG GTT CCC GAG TGC TTG AGC TGT GCG TCC CCG TGT AGC				
Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser				
398	407	416	425	434
TCT GAC CAG GTG GAA ACT CAA GCC TGC ACT CCG GAA CAG AAC CCG ATC TGC ACC				
Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys Thr				
452	461	470	479	488
TGC AGC CCC GCG TGG TAC TGC GCG CTG AUC AAG CAG GAG GGG TGC CCG CTG TGC				
Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys				
506	515	524	533	542
GCG CCG CTG CCG AAG TGC CCG CCG GCG TTC GCG GTG GCG AGA CCA GGA ACT GAA				
Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu				
560	569	578	587	596
ACA TCA GAC GTG GTG TGC AAG CCC TGT GCC CCG GGG AGC TTC TCC AAC ACG ACT				
Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Thr Thr				
614	623	632	641	650
TCA TCC ACG GAT ATT TGC AAG CCC CAC CAG ATC TGT AAC GTG GTG GCG ATC CCT				
Ser Ser Thr Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro				
668	677	686	695	704
GGG AAT GCA AGC AAG GAT GCA GTC TGC ACG TGC ACG TCC CCC ACC CCG AGT ATG				
Gly Asn Ala Ser Arg Asp Ala Val Cys Thr Ser Thr Ser Pro Thr Arg Ser MET				
722	731	740	749	758
GCC CCA GGG GCA GTA CAC TTA CCC CAG CCA GTG TCC ACA CCA TCC CAA CAC ACG				
Ala Pro Gly Ala Val His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr				
776	785	794	803	812
CAG CCA ACT CCA GAA CCC AGC ACT GCT CCA AGC ACC TCC TTC CTG CTC CCA ATG				
Gln Pro Thr Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro MET				
830	839	848	857	866
GGC CCC AGC CCC CCA GCT GAA GGG AGC ACT GCG GAC TTC GCT CTT CCA GTT GGA				
Gly Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Phe Ala Leu Pro Val Gly				
884	893	902	911	920
CTG ATT GTG GGT GTG ACA GCC TTG GGT CTA CTA ATA ATA GGA GTG GTG AAC TGT				
Leu Ile Val Gly Val Thr Ala Leu Gly Leu Leu Ile Ile Gly Val Val Asn Cys				
938	947	956	965	974
GTC ATC ATG ACC CAG GTG AAA AAG AAG CCC TTG TGC CTC CAG AGA GAA GCC AAG				
Val Ile MET Thr Gln Val Lys Lys Lys Pro Leu Cys Leu Gln Arg Glu Ala Lys				
992	1001	1010	1019	1028
GTG CCT CAC TTG CCT GCC GAT AAG GCG CCG GGT ACA CAG AGC CCC GAG CAG CAG				
Val Pro His Leu Pro Ala Asp Lys Ala Arg Gly Thr Gln Gly Pro Glu Gln Gln				

Figure
39

1044 1059 1064 1073 1082
CAC CTG CTG ATC ACA GCG CCG AGC TCC AGC AGC AGC TCC CTG GAG AGC TCG GCC
His Leu Leu Ile Thr Ala Pro Ser Ser Ser Ser Ser Ser Leu Glu Ser Ser Ala

1100 1109 1118 1127 1136 1145
AGT GCG TTT GAC AGA AGG GCG CCC ACT CCG AAC CAG CCA CAG GCA CCA GCG GTG
Ser Ala Leu Asp Arg Arg Ala Pro Thr Arg Asn Gln Pro Gln Ala Pro Gly Val

1154 1163 1172 1181 1190 1199
GAG GCC AGT GGG GCG GGG GAG GCG CCG GCC AGC ACC GGG AGC TCA GAT TCT TCC
Glu Ala Ser Gly Ala Gly Glu Ala Arg Ala Ser Thr Gly Ser Ser Asp Ser Ser

1208 1217 1226 1235 1244 1253
CCT GGT GGC CAT GGG ACC CAG CTC AAT GTC ACC TGC ATC GTG AAC CTC TGT AGC
Pro Gly Gly His Gly Thr Gln Val Asn Val Thr Cys Ile Val Asn Val Cys Ser

1262 1271 1280 1289 1298 1307
AGC TCT GAC CAC AGC TCA CAG TGC TCC TCC CAA GCC AGC TCC ACA ATG GGA GAC
Ser Ser Asp His Ser Ser Gln Cys Ser Ser Gln Ala Ser Ser Thr MET Gly Asp

1316 1325 1334 1343 1352 1361
ACA GAT TCC AGC CCC TCG GAG TCC CCG AAG GAC GAG CAG CTC CCC TTC TCC AAG
Thr Asp Ser Ser Pro Ser Glu Ser Pro Lys Asp Glu Gln Val Pro Phe Ser Lys

1370 1379 1388 1397 1406 1415
GAG GAA TGT GCG TTT CCG TCA CAG CTG GAG ACC CCA GAG ACC CTG CTG GGG AGC
Glu Glu Cys Ala Phe Arg Ser Gln Leu Glu Thr Pro Glu Thr Leu Leu Gly Ser

1424 1433 1442 1451 1460 1469
ACC GAA GAG AAG CCC CTG CCC CTT GGA GTG CCT GAT GCT GUG ATG AAG CCC AGT
Thr Glu Glu Lys Pro Leu Pro Leu Gly Val Pro Asp Ala Gly MET Lys Pro Ser

1478 1488 1498 1508 1518 1528 1538
TAA CCAGGCCGGT GTGGGCTGTG TCGTAGCCAA GGTGGGCTGA GCCCTGGCAG GATGACCCTG

1548 1558 1568 1578 1588 1598 1608
CGAAGGCGCC CTGCTCTTC CAGGCCCCCA CCACTAGGAC TCTGAGGCTC TTCTGAGCC AAGTTCCTCT

1618 1628 1638 1648 1658 1668 1678
AGTGCCTCC ACAGCCGCA GCTCCTCTG ACCTGCAGGC CAAGAGCAGA GGCAGCGGT TGTGGAAAGC

1688 1698 1708 1718 1728 1738 1748
CTCTGCTGCC ATGGTGTGTC CCTCTCGAA GGTGCTGTC GCATGGACGT TCAGGCGATG CTGGGCAAG

1758 1768 1778 1788 1798 1806 1818
TCCCTUACTC TGTGTGACCT GCGCGCCCA GCTGCACCTG CCAGCCTGCG TTCTGAGCC CTTGGUTTTT

1828 1838 1848 1858 1868 1878 1888
TTGTTTGT TTGTTTGT TTGTTTGT CTCGCCCTG GCTCTGCCCC AGCTCTGCT TCCAGAAAAC

1898 1908 1918 1928 1938 1948 1958
CCCAGCATCC TTCTCTGAG AGGGGCTTTC TGGAGAGGAG GGATGCTGCC TGAGTCACCC ATGAGGACAG

1968 1978 1988 1998 2008 2018 2028
GACAGTGCTT CAGCCTGAGG CTGAGCTGC GGGATGCTCC TGGGCTCTG TGCAGGAGG AGGTGGCAGC

2038 2048 2058 2068 2078 2088 2098
CCTGTAGGGA ACUGGCTCCT TCAAGTTAGC TCAGGAGCT TGGAAAGCAT CACCTCAGGC CACTGTGCCC

2108 2118 2128 2138 2148 2158 2168
ACCCGATTT AACTCTTTT TCTCCCAAT GGGATATAG GACCTGCTC TTCTATCAG AAAAGGAGAT

2178 2188 2198 2208 2218
TGTGAGCAAG AGGCAATTA ATAATATG CCAAATATT AAAAAACCG AATTC

Figure
39 cont.

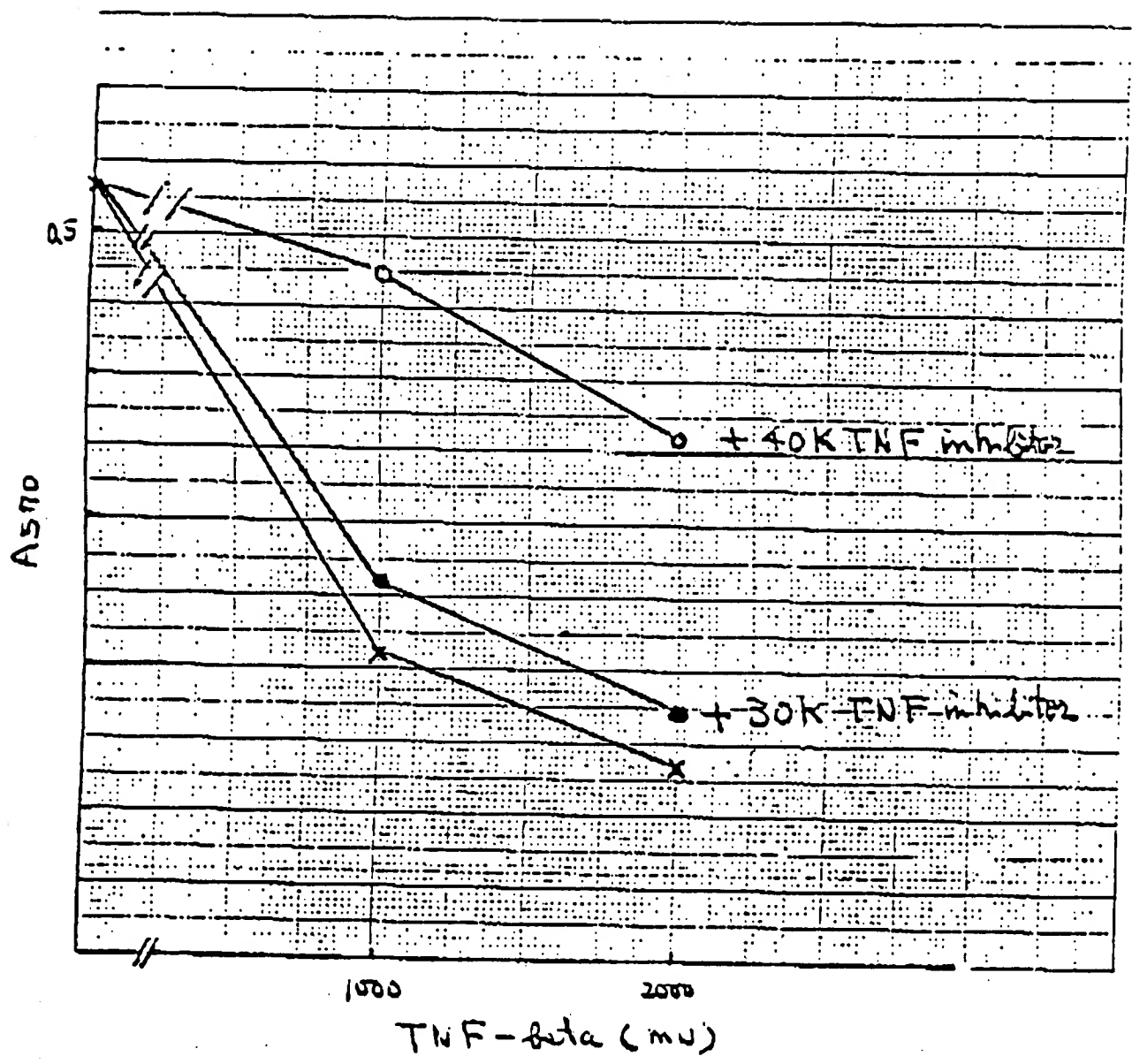


Figure 40

Figure 41

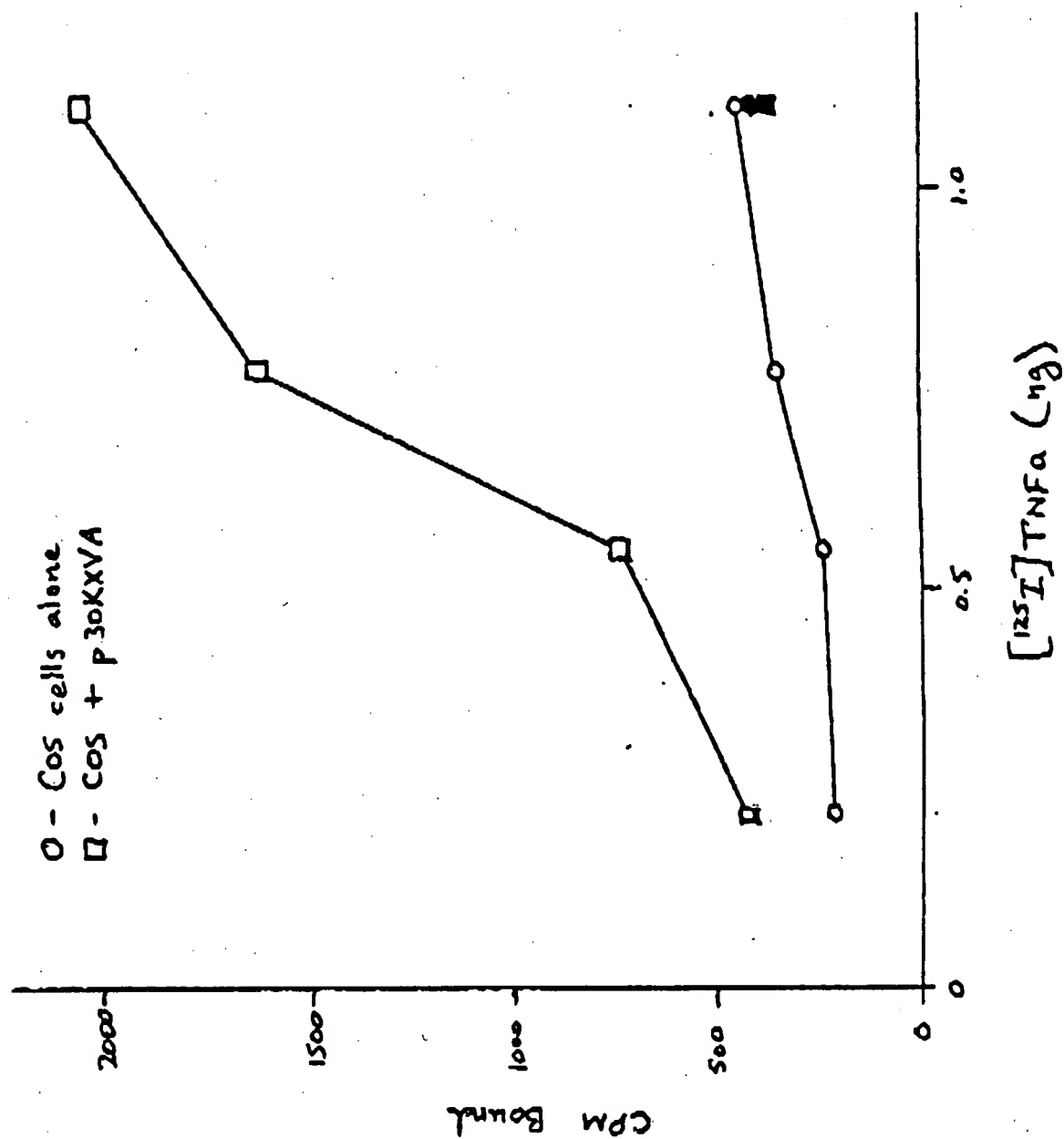
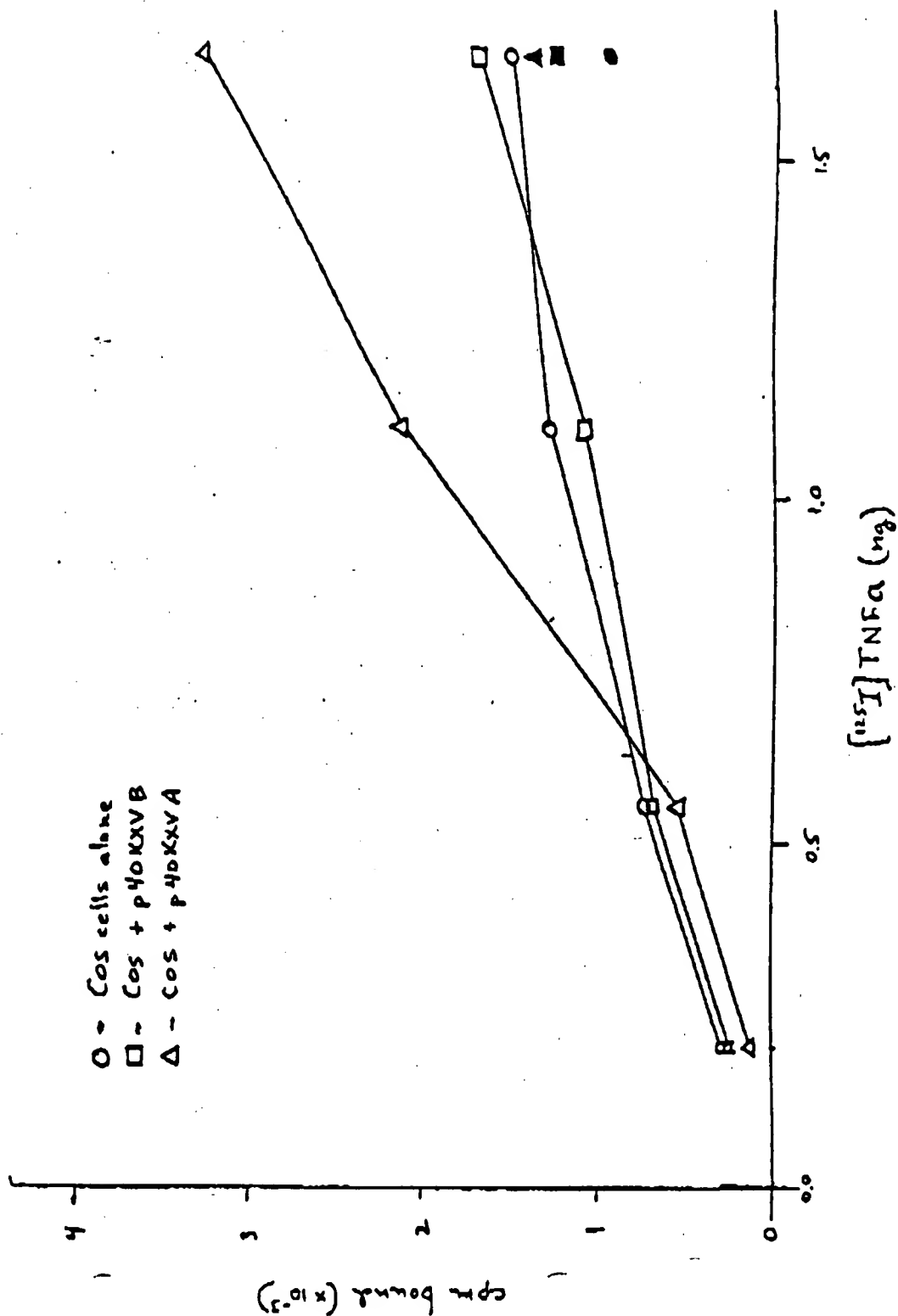


Figure 42



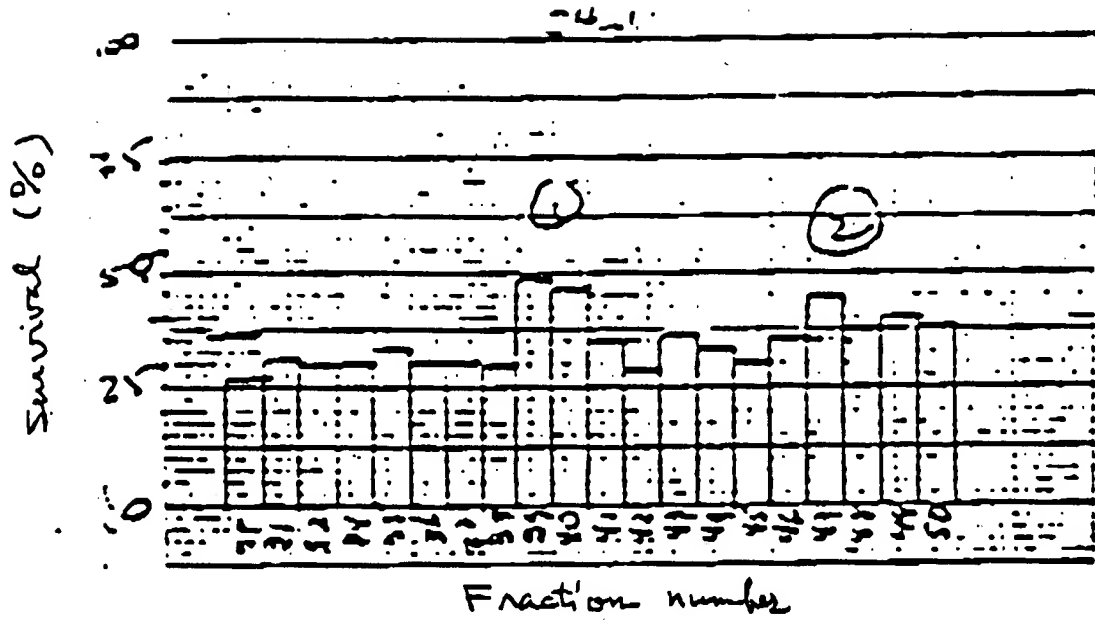


FIG 43

FIG 44

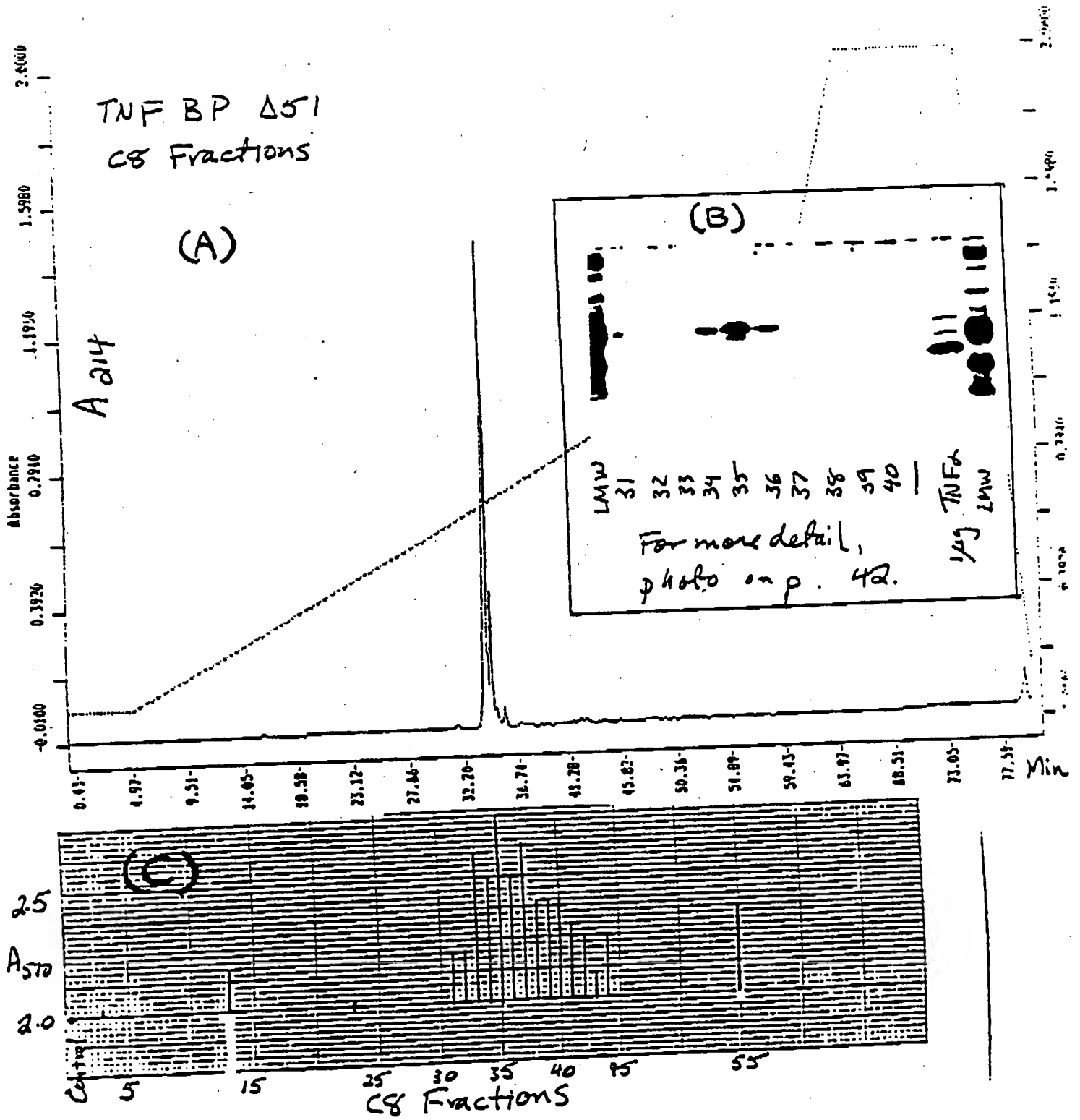


FIG. 45

